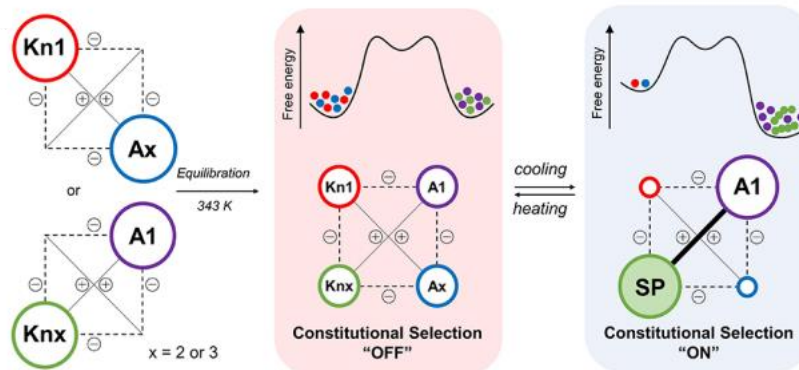
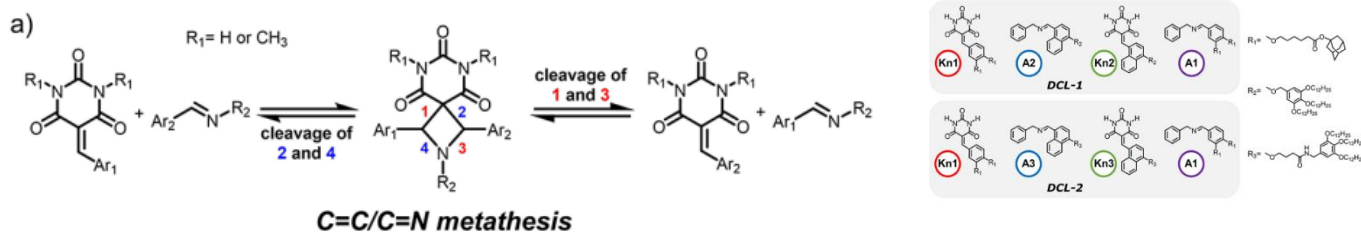


- (1) Gu, R.; Lehn, J.-M. Constitutional Dynamic Selection at Low Reynolds Number in a Triple Dynamic System: Covalent Dynamic Adaptation Driven by Double Supramolecular Self-Assembly. *J. Am. Chem. Soc.* **2021**, *143* (35), 14136–14146. <https://doi.org/10.1021/jacs.1c04446>.



^aFor Ax and Knx, x = 2 or 3.



Who are the corresponding authors and what are their research areas?

Jean-Marie Lehn. His main research interest was in the field of organic chemistry and later became a pioneer in the field of supramolecular chemistry because of his deep investigation of engineering molecules on higher level of complexity. In 1968, he synthesized cages-like molecules (cryptands), in which he expanded the idea of “molecular recognition”. He was also interested in self-organization, and more recently he developed the concept of dynamic combinatorial chemistry: a system that undergo with different thermodynamic equilibrium states in response to external effector. His famous dynamic system is composed of imine libraries, a variety of imine molecules that exchange their building blocks between each other’s relying on their reversibility of formation and dissociation.

What is the main claim of the article?

A demonstration of a dynamic library adaptation through a double self-assembly showing temperature as key parameter to switch on-off the constituents distribution of the library. In addition to previous effects, they claimed that lowering the Reynolds number of the medium due to gel formation, it can also be considered as additional environmental effector for the amplification of selective constituents.

How is it demonstrated?

Equimolar amount of starting material was used in both direction of the equilibrium reaction, and the mixture is equilibrated before proceeding with the external effector (temperature variation). Using ¹H-NMR (500 MHz), by integration they were able to calculate the relative composition of each constituent.

What are the typical experimental conditions?

The two reactants Kn1 and A3 (2 mM each) were mixed in 10% CDCl₃ + 90% CH₂-d₁₂ and equilibrated at 343 K to give a statistical distribution of four constituents (reactant+products). The library is then cooled down to 293 K. Then a mixture of chloroform and cyclohexane with different ratio is used to prove the effect of the medium

polarity on the amplification at equilibrium.

Which are the key related papers?

- 1) Giuseppone, N.; Lehn, J.-M. Protonic and Temperature Modulation of Constituent Expression by Component Selection in a Dynamic Combinatorial Library of Imines. *Chem. Eur. J.* **2006**, *12* (6), 1715–1722. <https://doi.org/10.1002/chem.200501038>.
- 2) Huc, I.; Lehn, J.-M. Virtual Combinatorial Libraries: Dynamic Generation of Molecular and Supramolecular Diversity by Self-Assembly. *Proc. Natl. Acad. Sci. U.S.A.* **1997**, *94* (6), 2106–2110. <https://doi.org/10.1073/pnas.94.6.2106>.

Additional comments, including additional elements of interest

This manuscript showed clearly an example of a molecular selection induced by the medium using simple library composed of imines and Knoevenagel. This library is so fast to reach equilibrium state because it can undergo with an associative mechanism instead of dissociative.