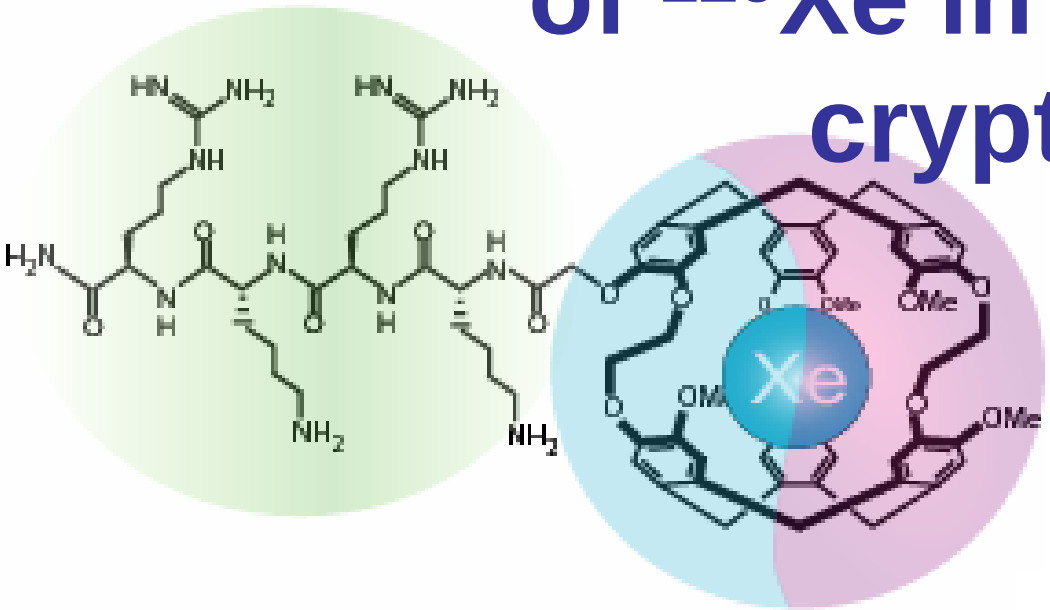
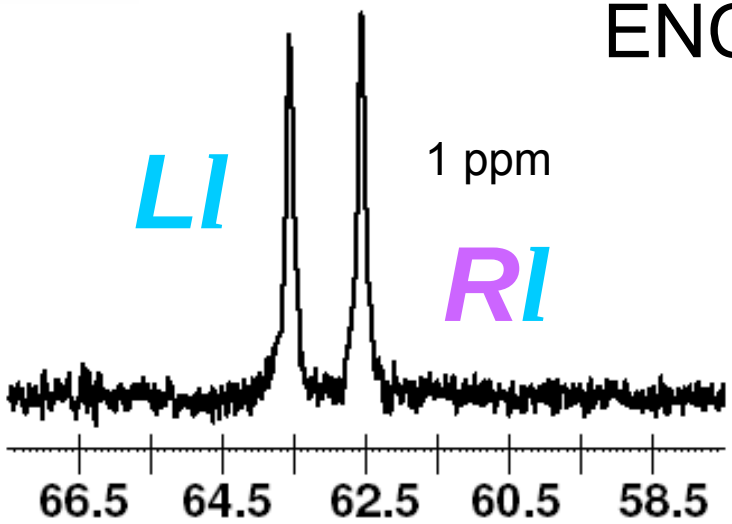
Diastereomeric chemical shifts of ^{129}Xe in functionalized cryptophane cages.



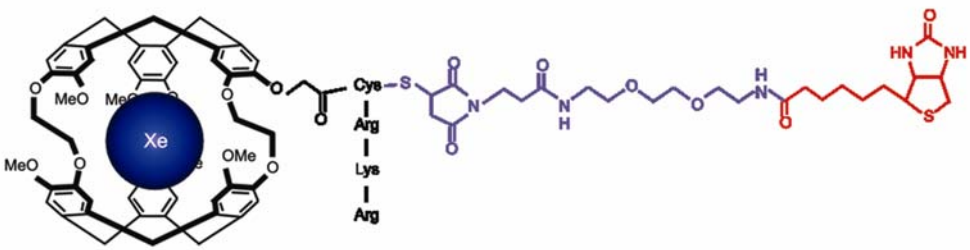
E. J. Ruiz, A. Pines
D. N. Sears, and
C J. Jameson

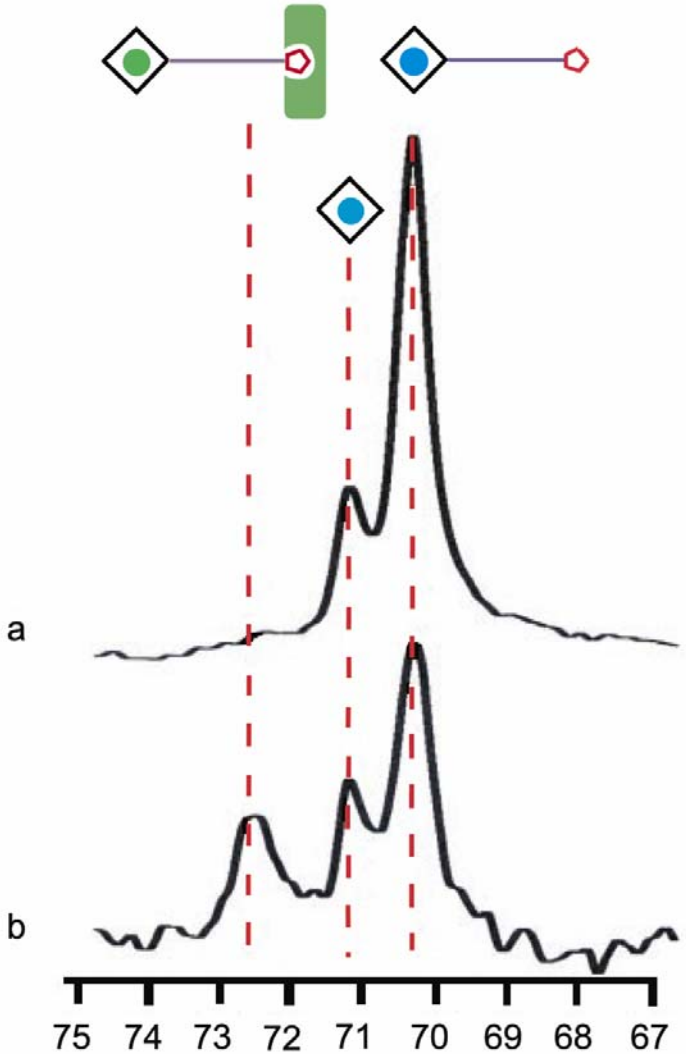
ENC 2005

Now we can assign the experimentally observed Xe signals to the specific member of the diastereomeric set

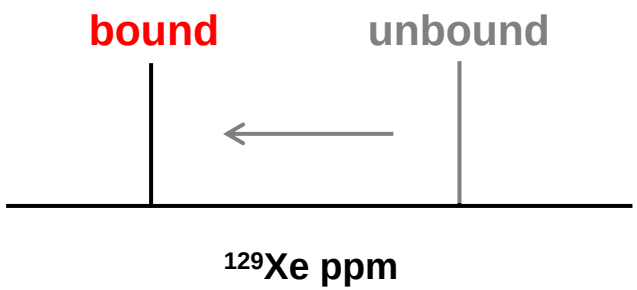


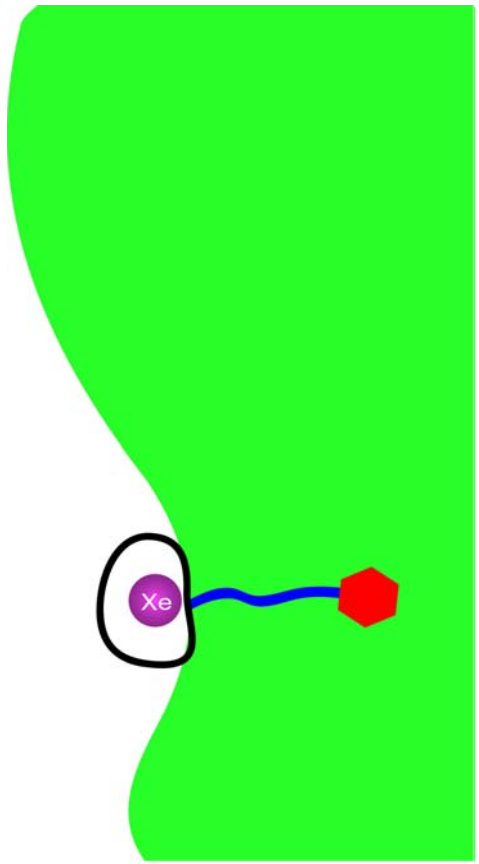
Functionalization of the cryptophane-A cage paved the way in developing a xenon-cryptophane guest-host complex which has demonstrated biosensing capabilities.

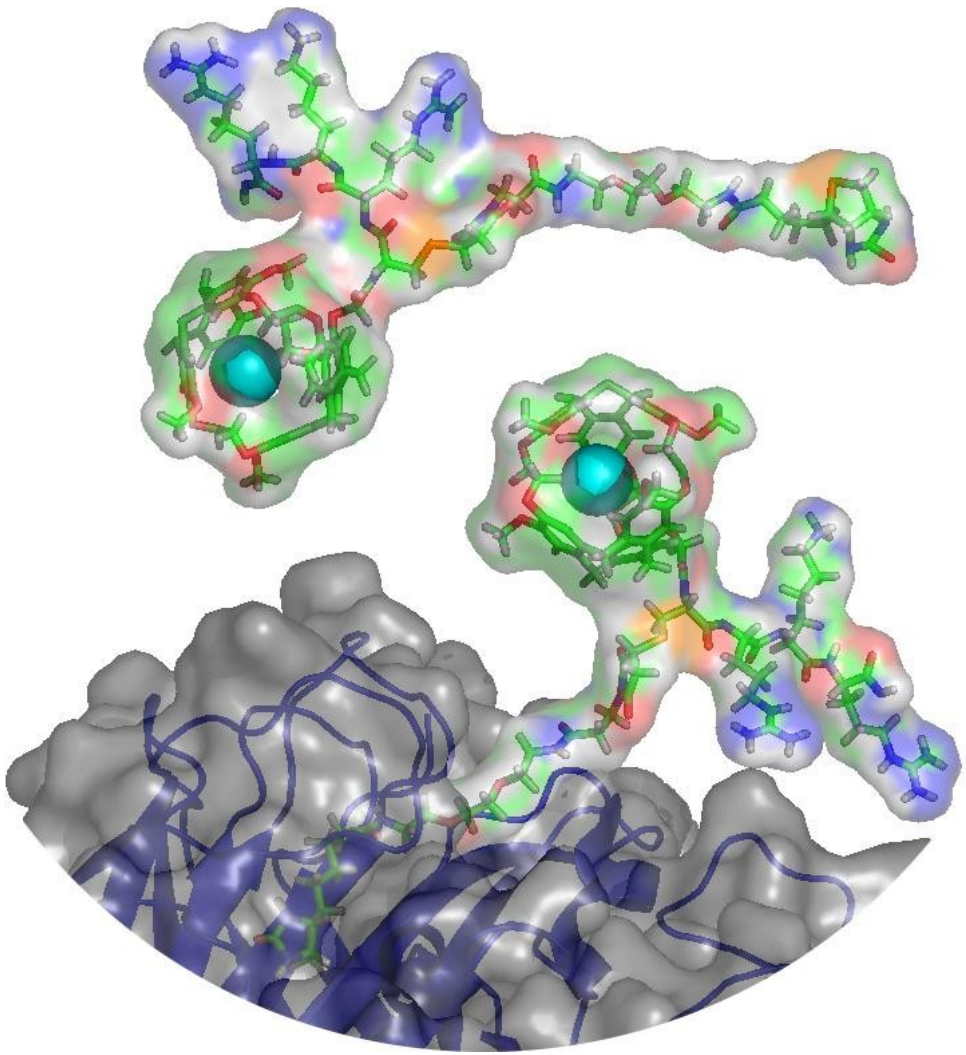




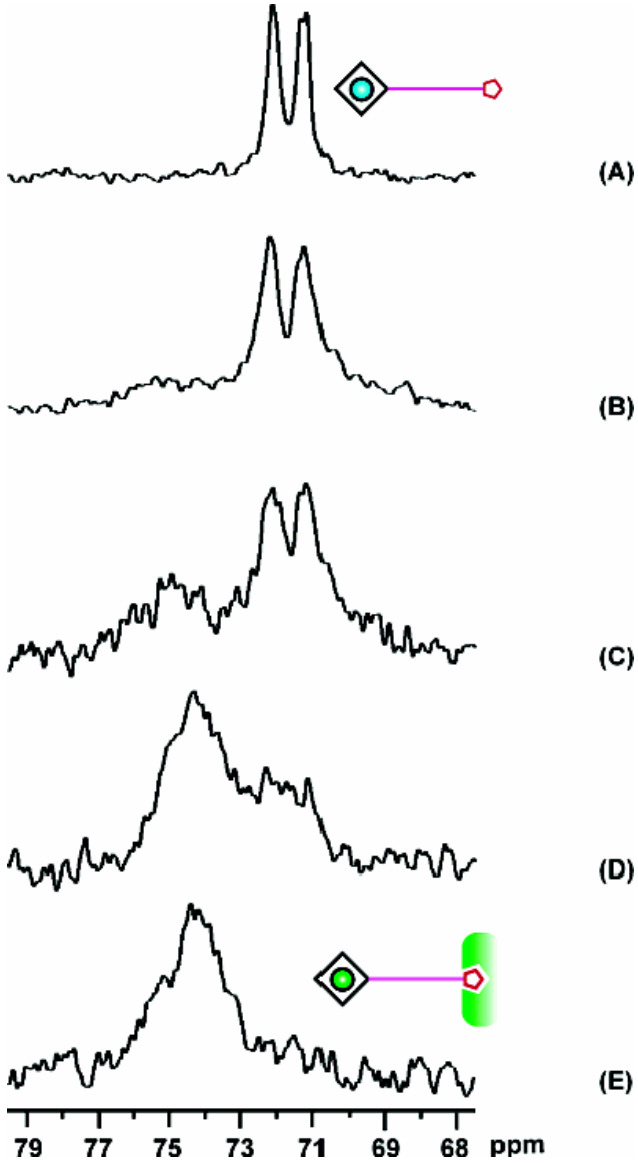
M.M. Spence, S.M. Rubin, I.E. Dimitrov, E.J. Ruiz, D.E. Wemmer, A. Pines, S.Q. Yao, F. Tian, and P.G. Schultz Proc. Nat. Acad. Sci. **2001**, 98, 10654-657.


bound
unbound
^{129}Xe ppm


Xe



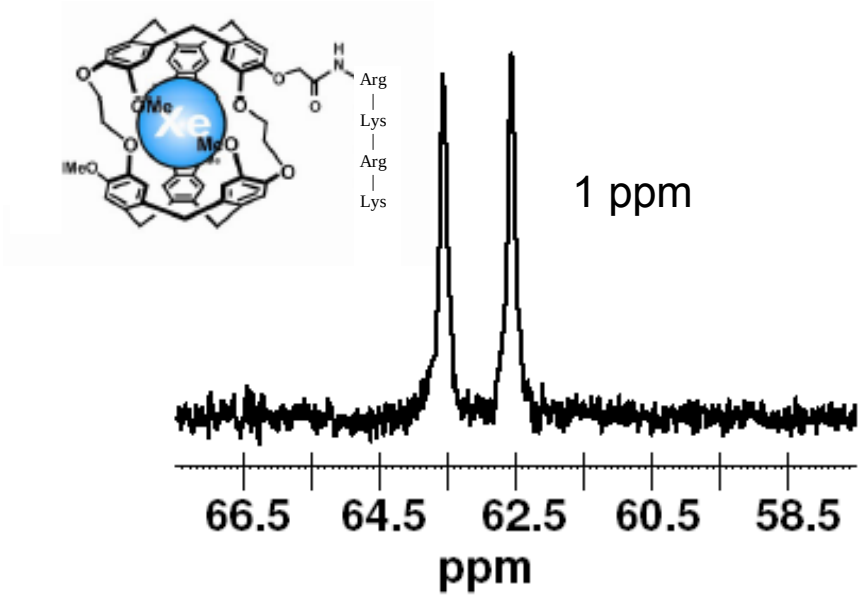
model courtesy of T. J. Lowery



M. M. Spence, E. J. Ruiz, S. M. Rubin,T. J. Lowery, N. Winssinger, P. G. Schultz, D. E. Wemmer, A. Pines, J. Am. Chem. Soc. 126, 15287 (2004)

Xe signal is split

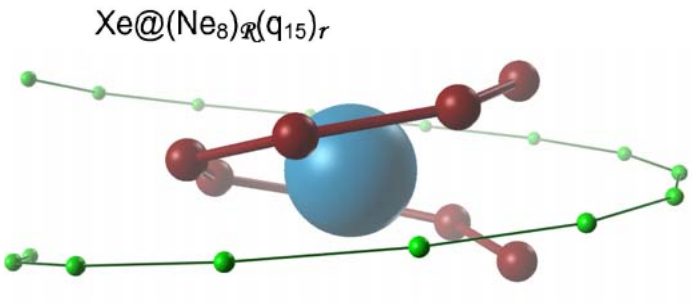
With D_{3d} symmetry, the cryptophane-A cage is **chiral**. When a further chiral functional group is substituted onto the cryptophane-A cage, the ^{129}Xe NMR signal from the xenon sequestered within the cage is split into two or more peaks.

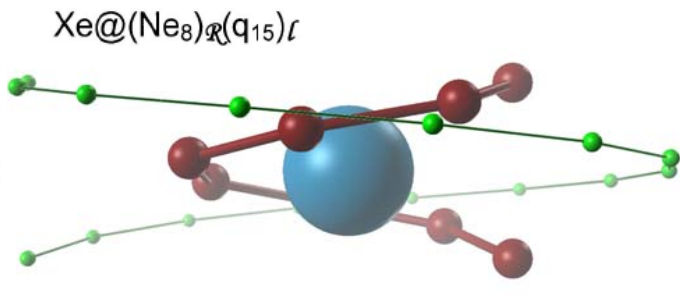


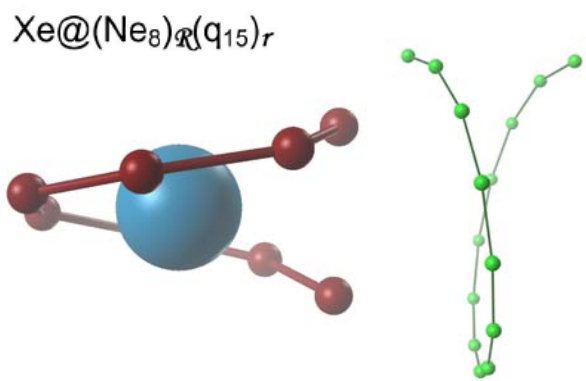
M. M. Spence, E. J. Ruiz, S. M. Rubin,T. J. Lowery, N. Winssinger, P. G. Schultz, D. E. Wemmer, A. Pines, J. Am. Chem. Soc. 126, 15287 (2004)

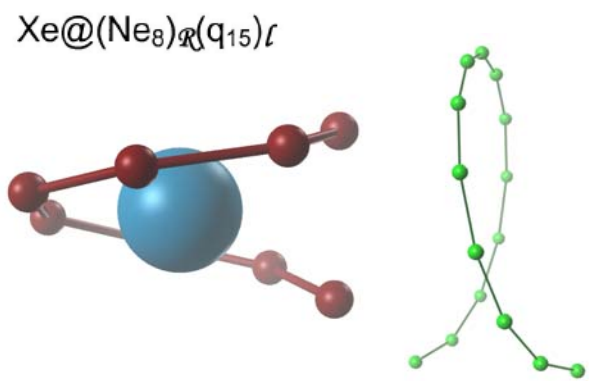
To understand diastereomeric shifts of Xe we studied model systems:

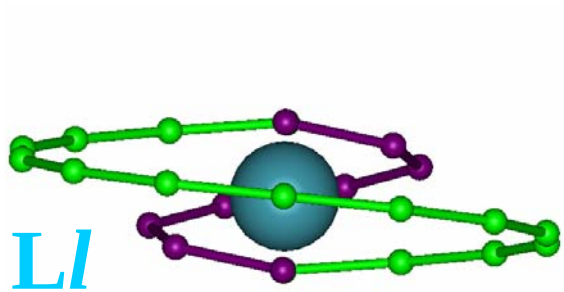
Xe in helical arrangements of atoms and partial charges at coaxial or perpendicular configurations, to establish that the chiral nature of real tethers can be modeled by differently oriented partial charges

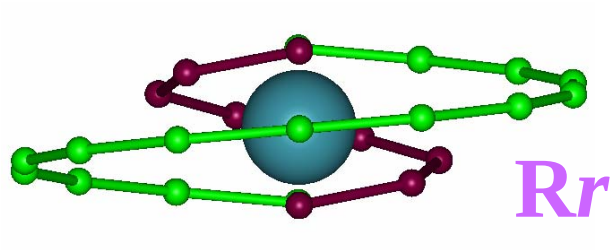




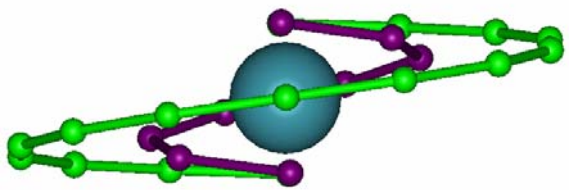


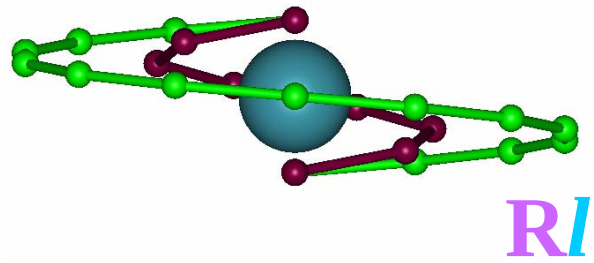






$Xe@Ne_8(+q)_{15}$



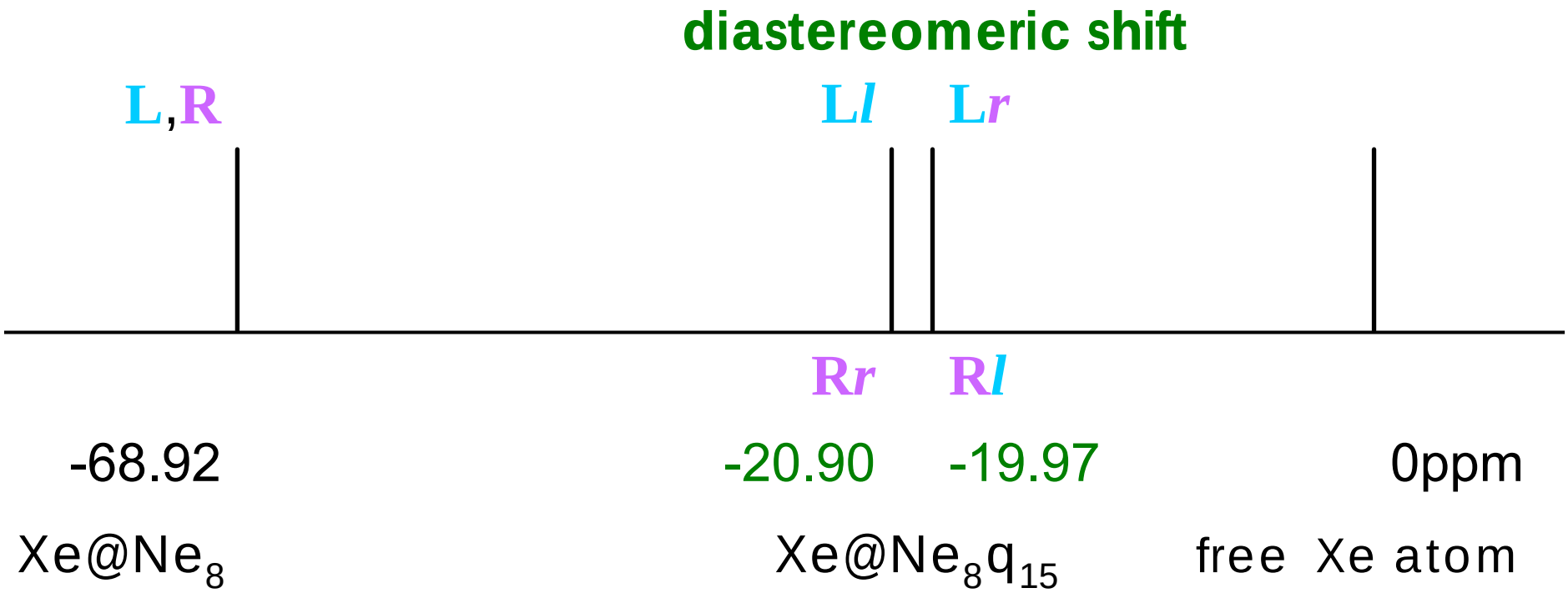


L*l* and R*r* are mirror images

L*r* and R*l* are mirror images

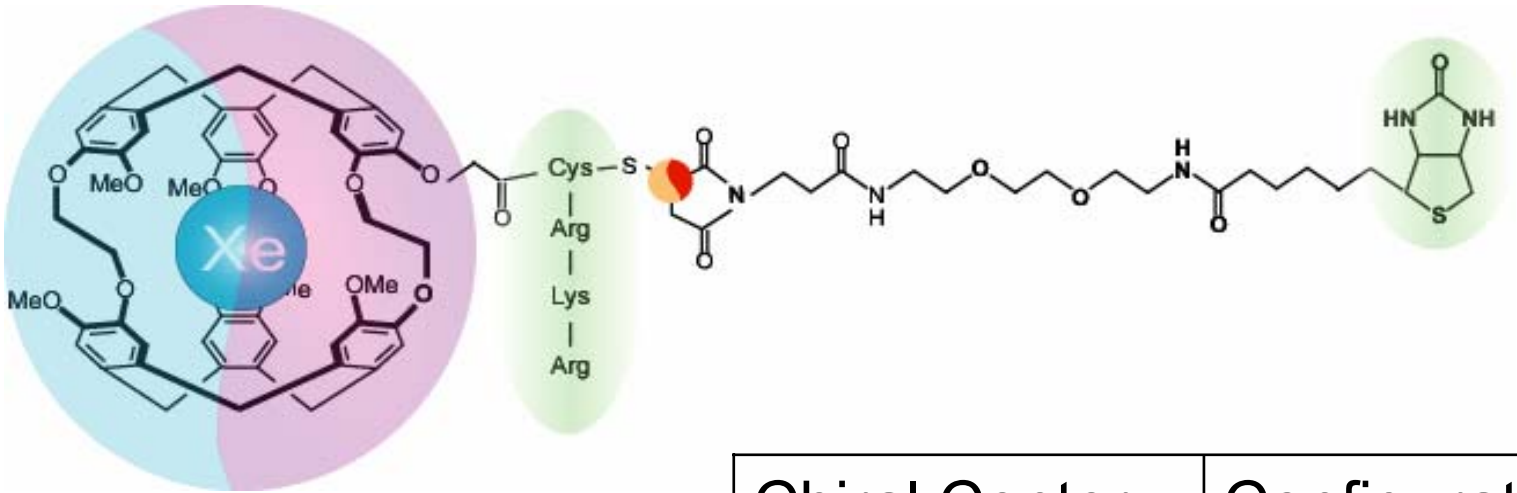
L*l* and L*r* are diastereomers

^{129}Xe NMR spectrum of Xe in Ne helices



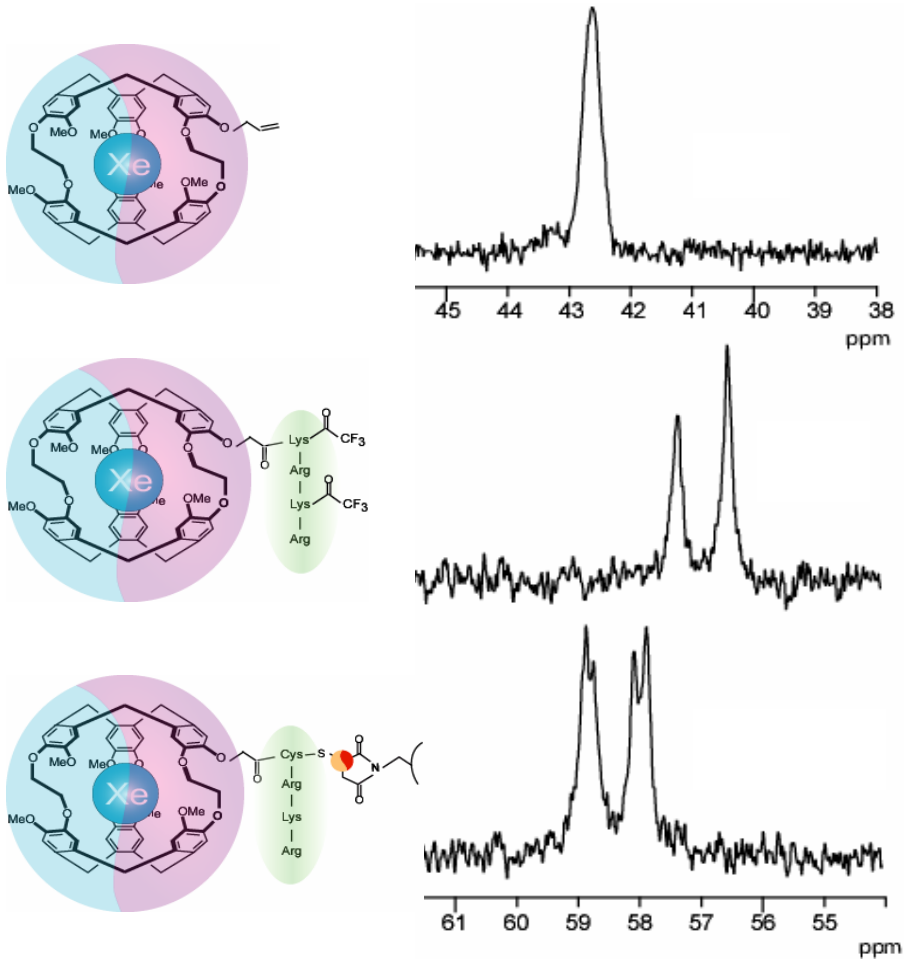
D.N. Sears, C. J. Jameson, R. A. Harris, J. Chem. Phys. 119, 2685 (2003)

Chiral Components of the biosensor



Chiral Center	Configuration			
Cage	L	L	R	R
Peptide	L	L	L	L
Asymmetric Carbon	L	R	L	R
Ligand	D	D	D	D

Diastereomeric Resolution
of biosensor precursors

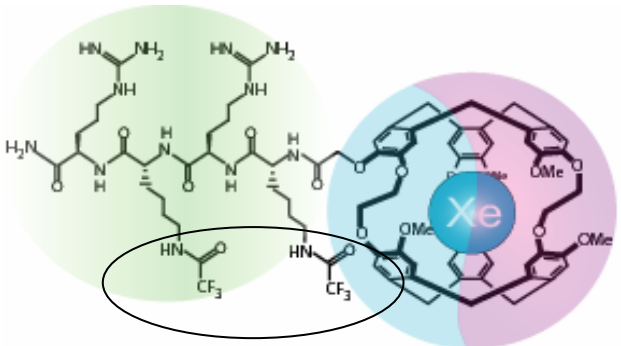


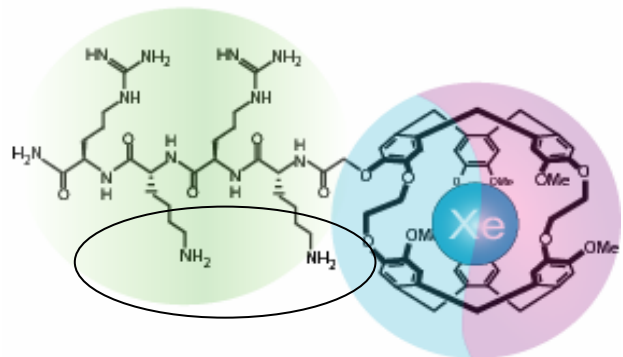
R and **L**

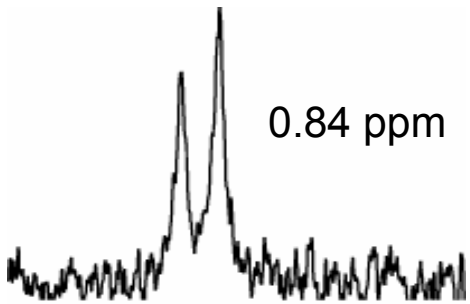
Rl and **L**l

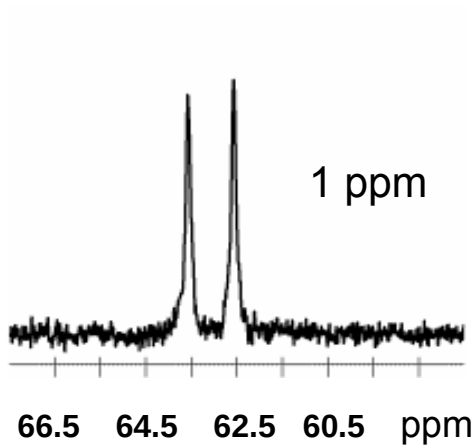
Rl*ℓ*, **L**l*ℓ*, **R**l*r*, and **L**l*r*

TFA Substitution

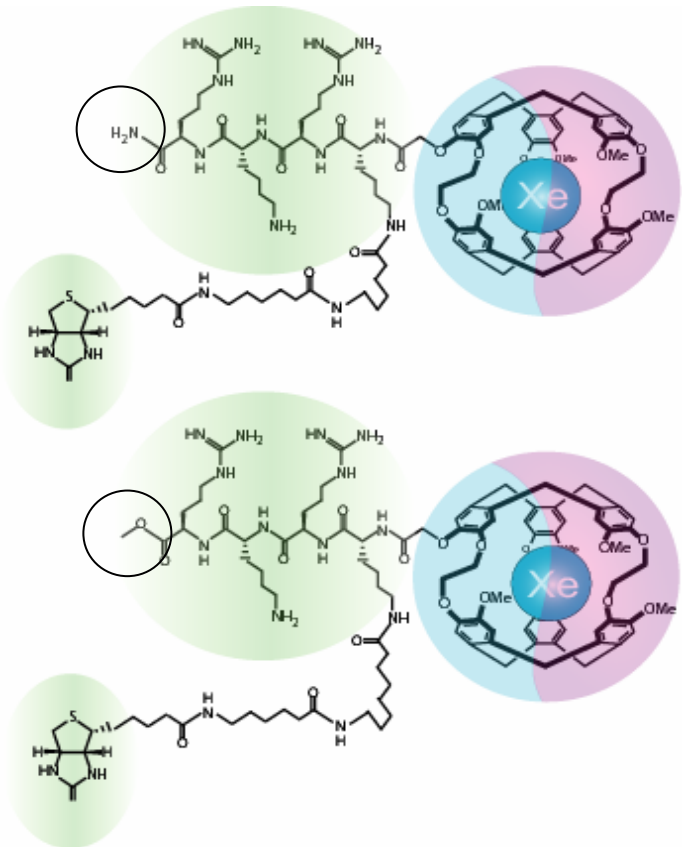


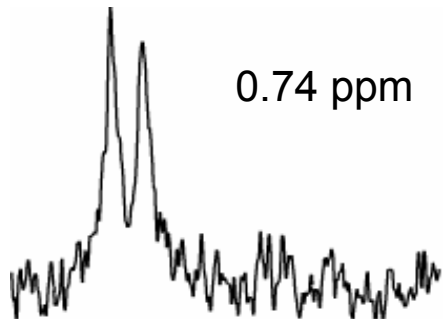


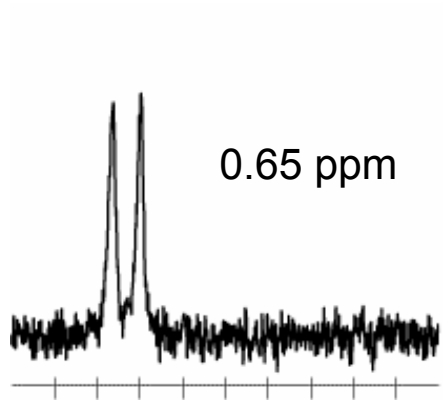




-NH_2 Substitution

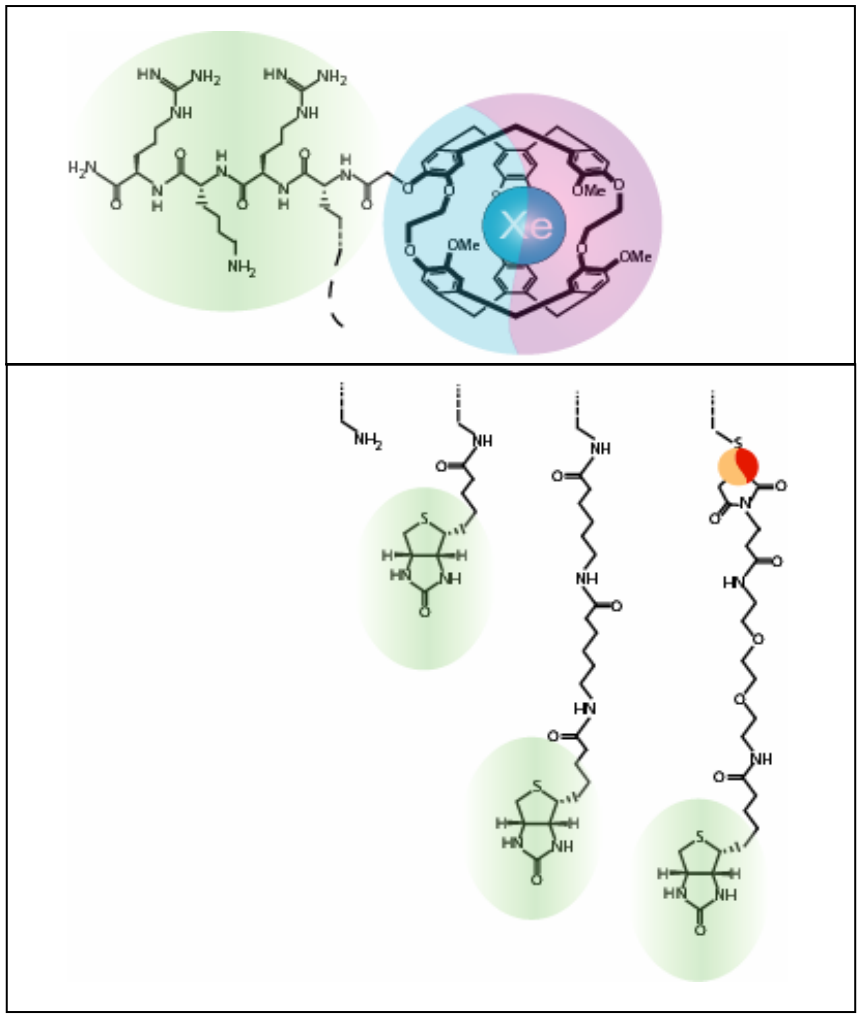


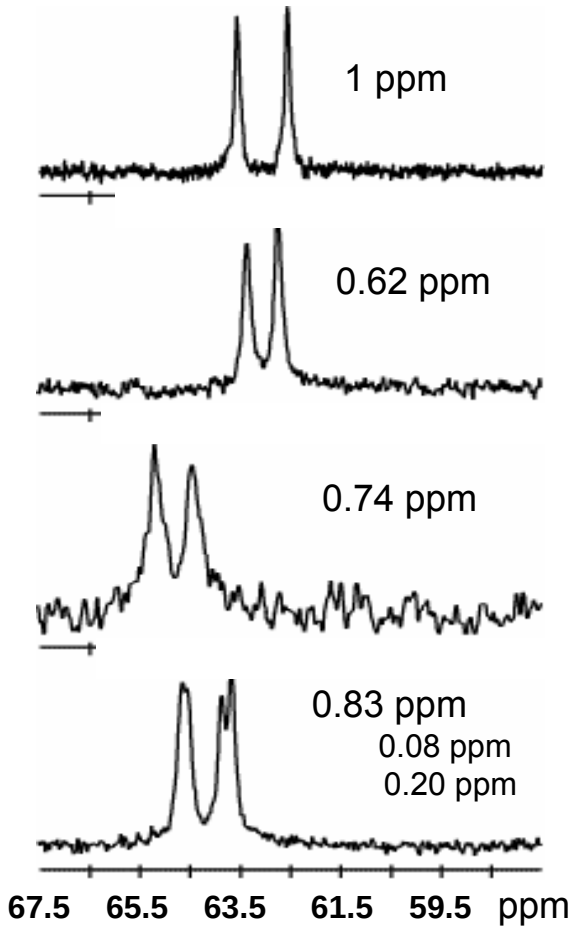




66.5 64.5 62.5 60.5 58.5 ppm

More examples:





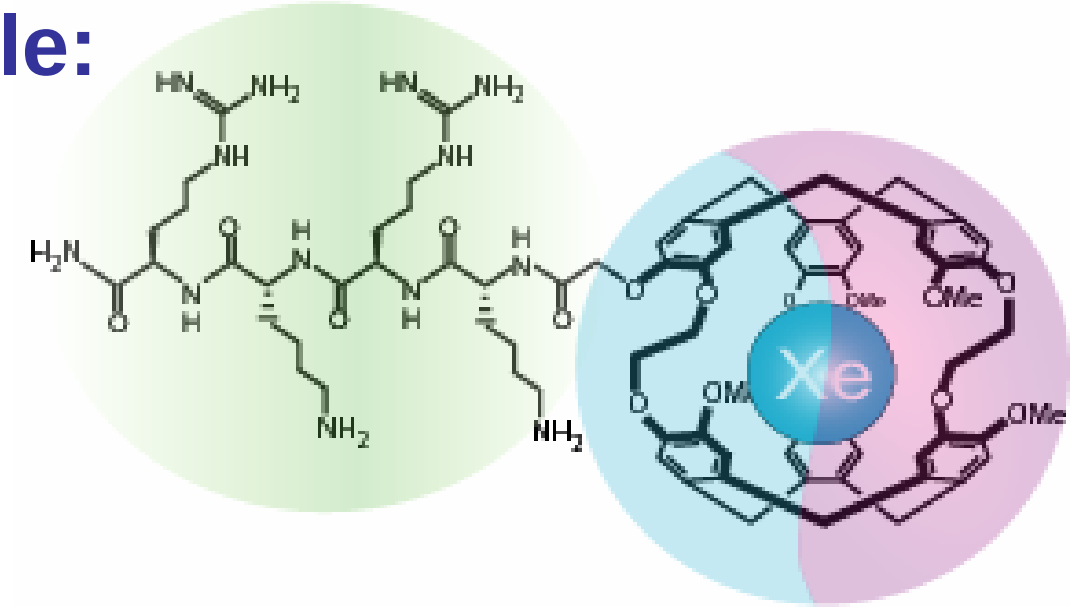
Diastereomerism of functionalized cages

chiral components		diastereomers	
cage	amino acids	configuration	**same σ** ⊙
R	***l***	***Rl***	***Lr***
L	***l***	***Ll***	***Rr***

⊙**Nuclear shieldings are related by symmetry**

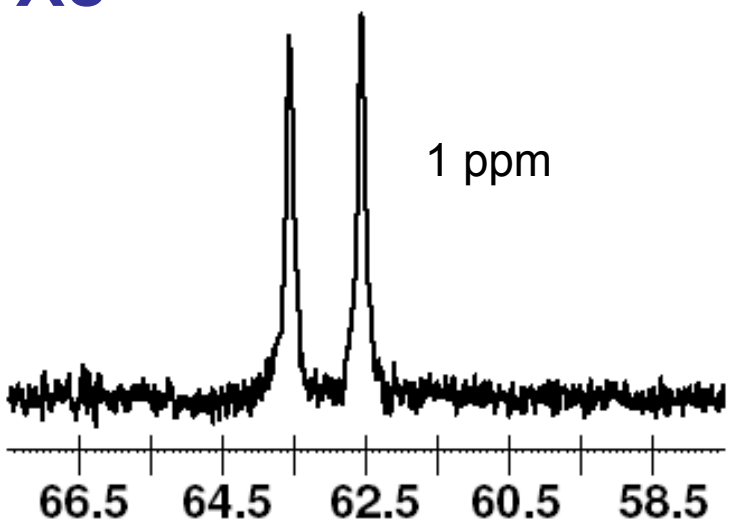
$\sigma(Rr) \equiv \sigma(Ll)$ and $\sigma(Rl) \equiv \sigma(Lr)$

Choose one example:

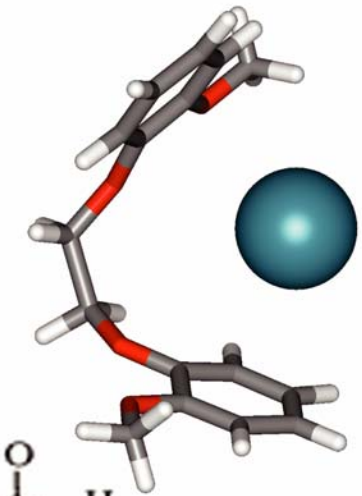


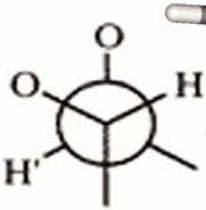
Experiment

^{129}Xe NMR spectrum of Xe in a functionalized cryptophane-A cage

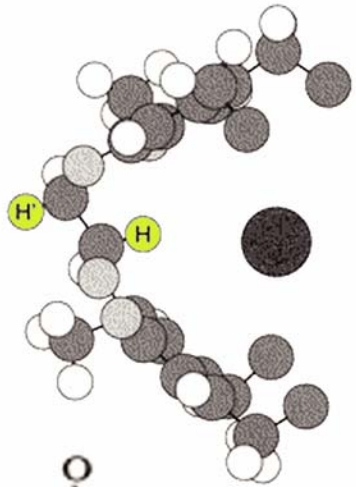


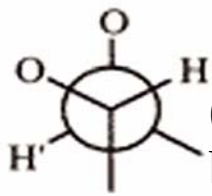
The average structure of Xe@cryptoA to be used for quantum calculations





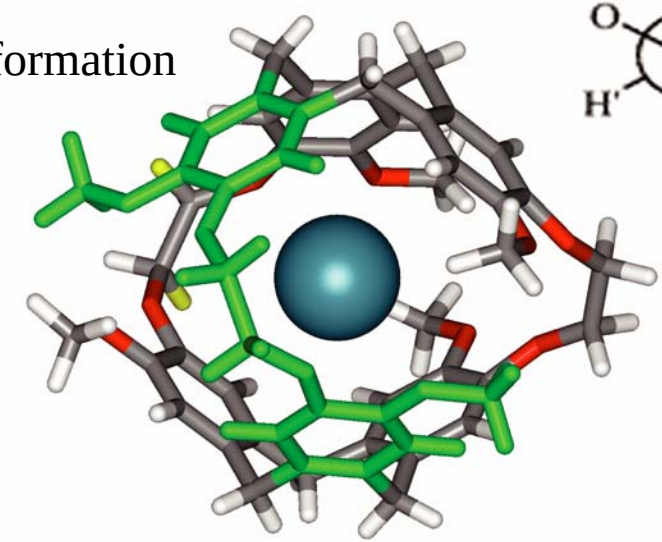
(d) conformation





(d) conformation based on SPINOE

M., Luhmer, B. M. Goodson, Y. Q. Song, D. D. Laws, L. Kaiser, M. C. Cyrier, and A. Pines
J. Am. Chem. Soc. **1999**, 121, 3503



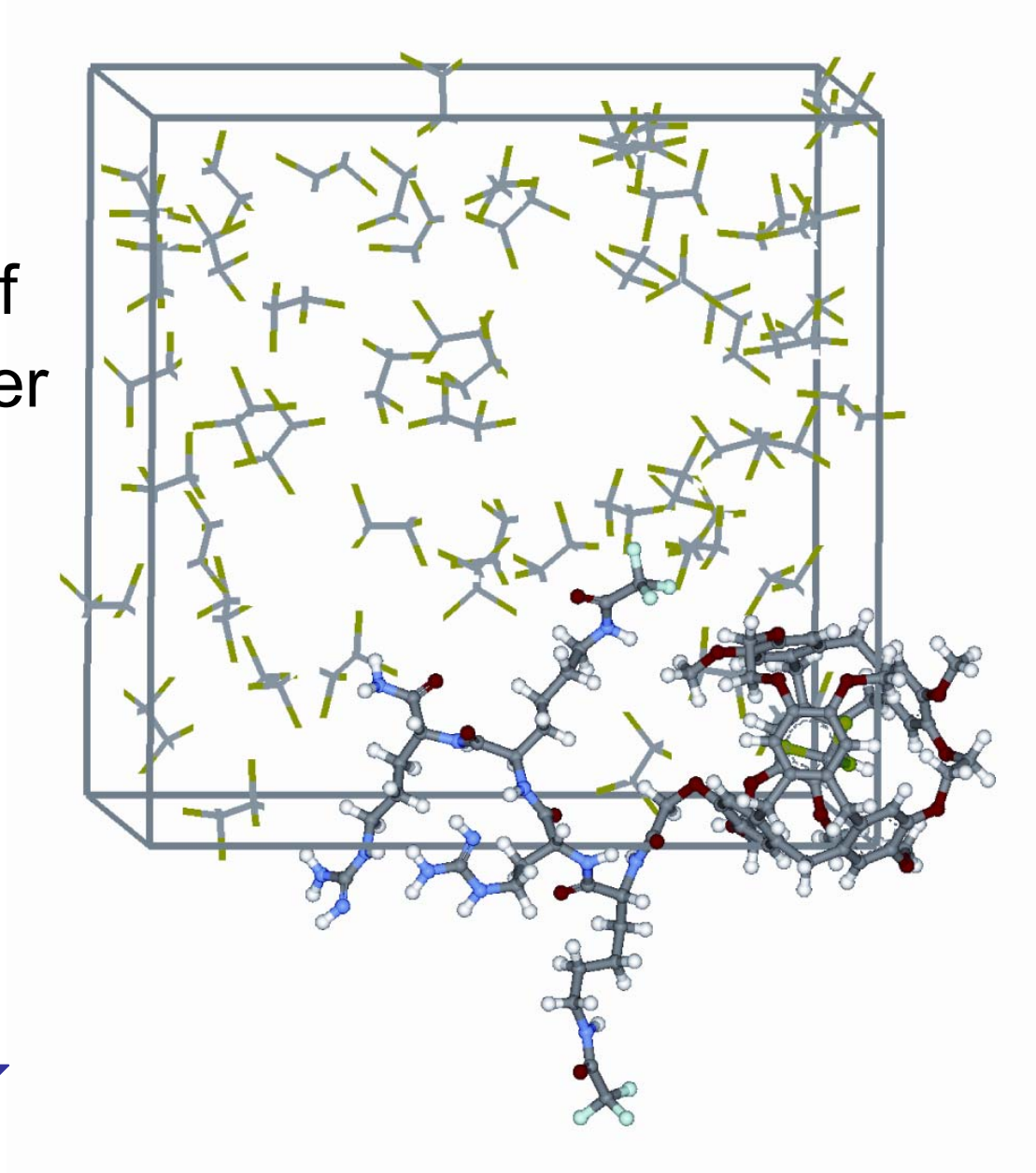
Minimum energy structure arrived at is completely consistent with SPINOE experiments

D. N. Sears, C. J. Jameson,
J. Chem. Phys. 119, 12231 (2003)

MOLECULAR DYNAMICS:

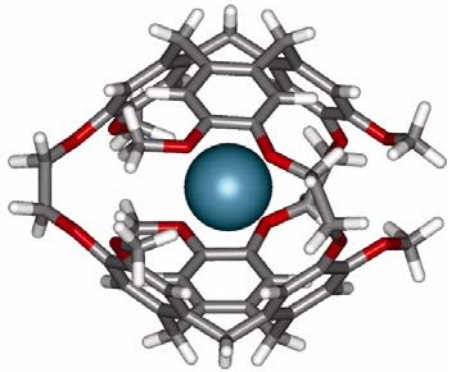
Molecular dynamics of cage with ***l*** (or ***r***) tether within a solvent box finds the equilibrium arrangement of the tether atoms relative to the cage for each member of the diastereomeric pair.

This is followed by

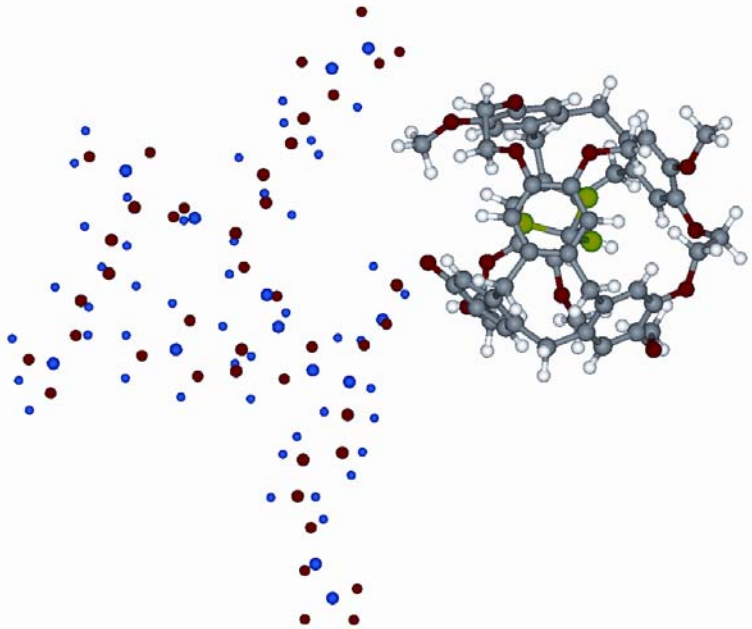


QUANTUM MECHANICAL CALCULATIONS of Xe SHIELDING

These nuclei and electrons are included in the QM calculations of Xe shielding:

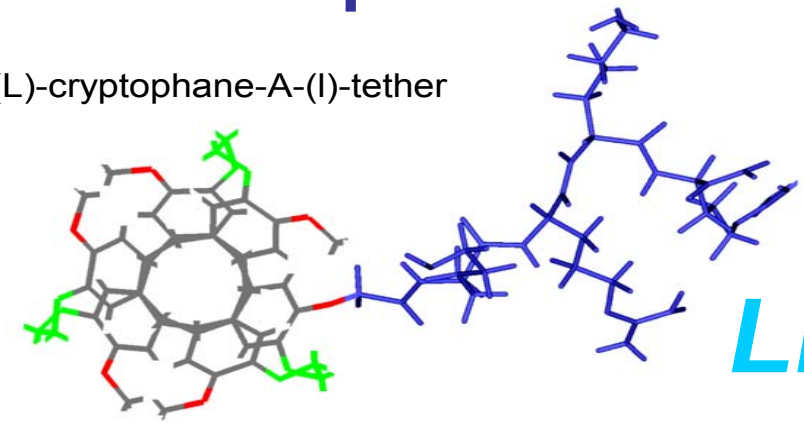


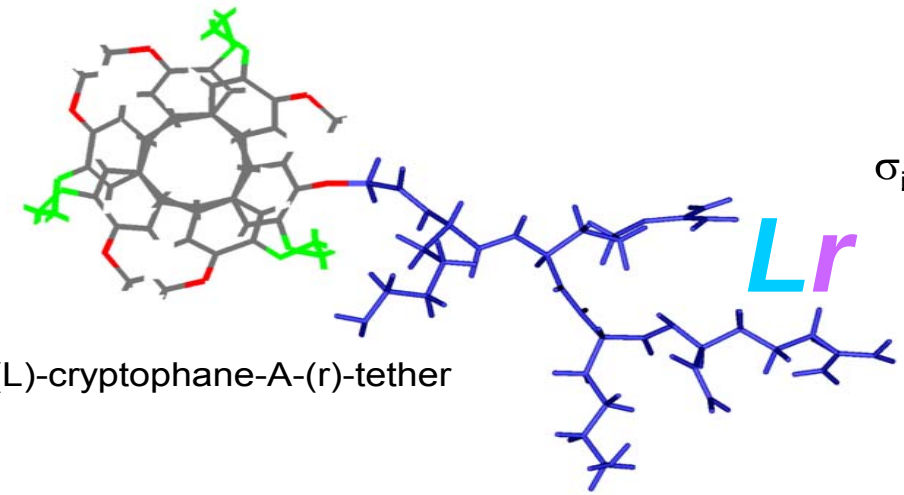
The ***l*** or ***r*** tether is included as a collection of point charges located at the equilibrium positions of the tether atoms:



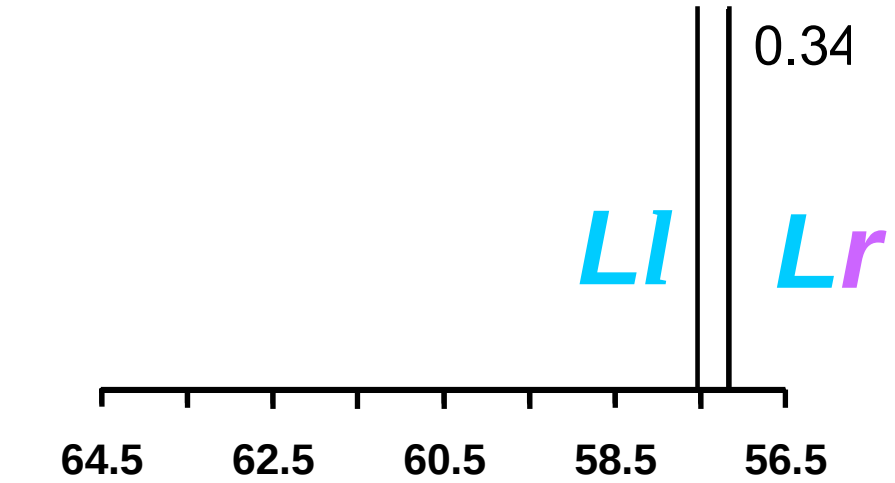
Quantum mechanical Xe shieldings for two spatial configurations of the amino acid tether with respect to the cryptophane-A cage

(L)-cryptophane-A-(l)-tether

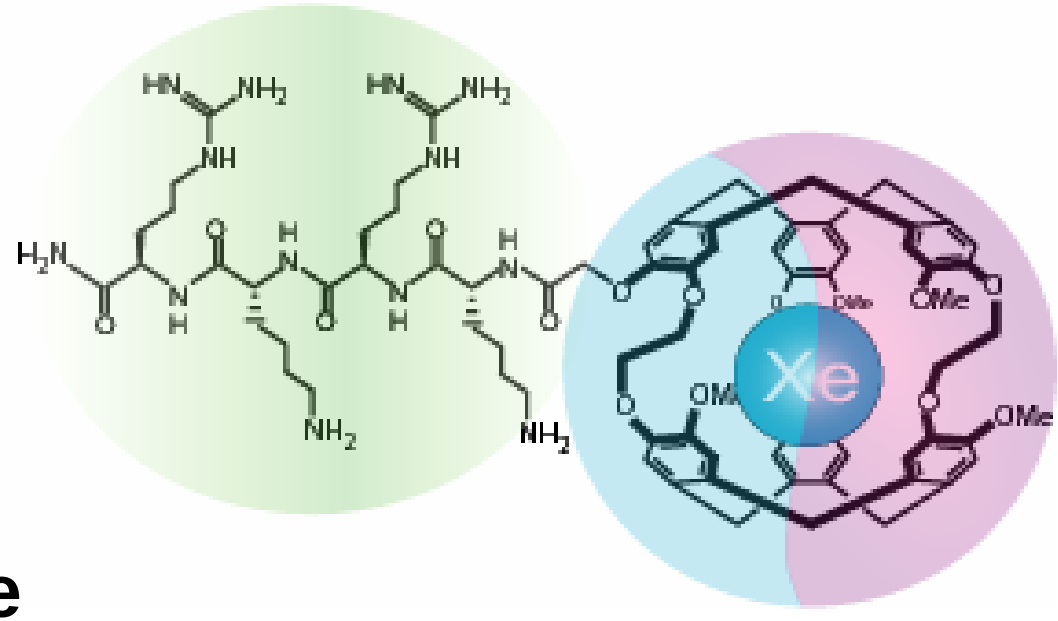




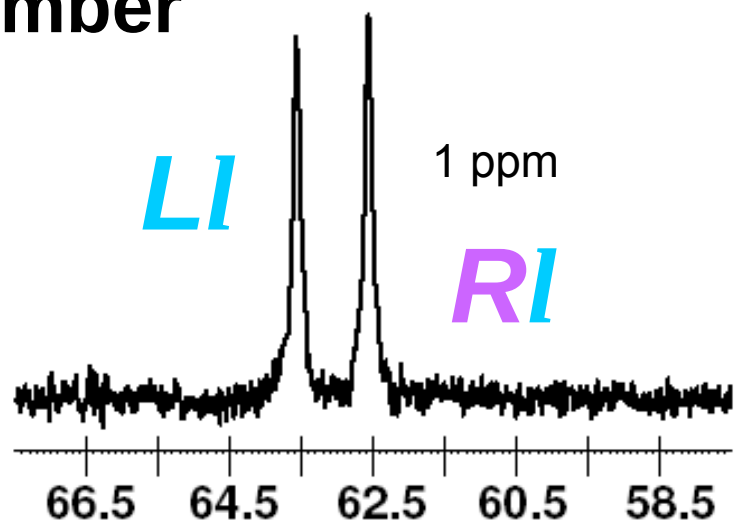
(L)-cryptophane-A-(r)-tether



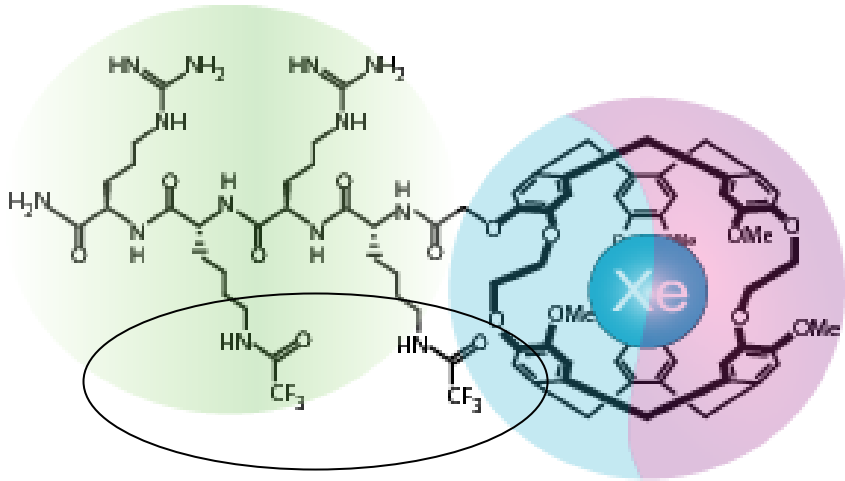
σ_{iso}(Xe@cryptophane-A-rkrk) – σ(free Xe atom)



Now we can assign the experimentally observed Xe signals to the specific member of the diastereomeric set



Choose a second example:



Experiment

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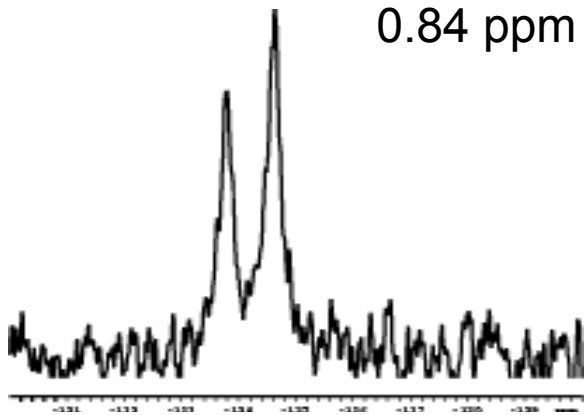
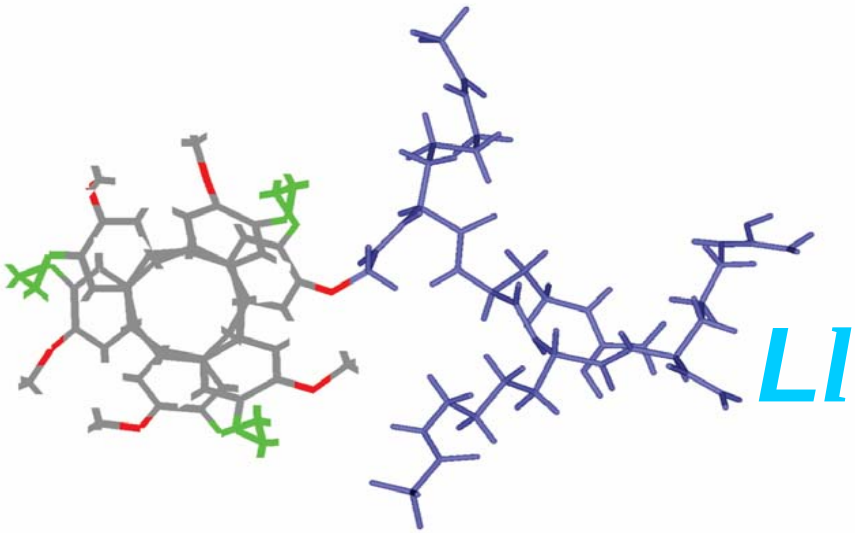
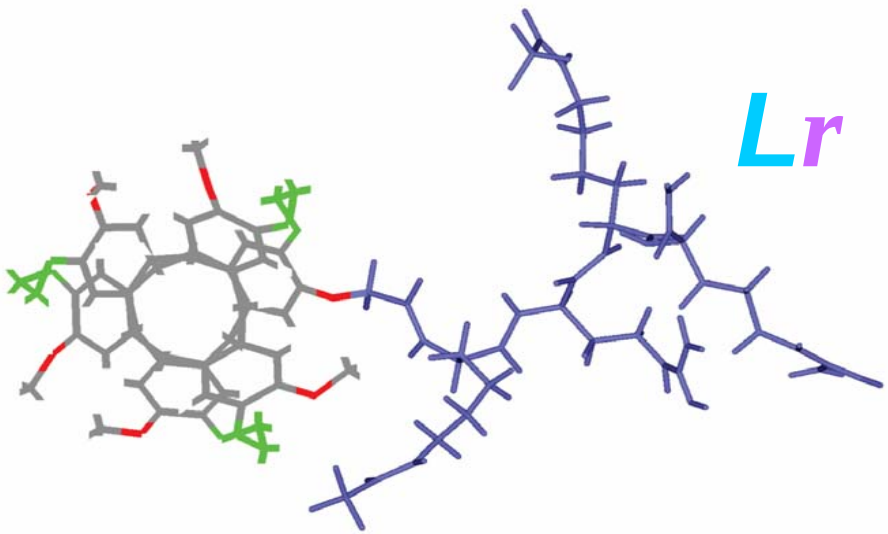


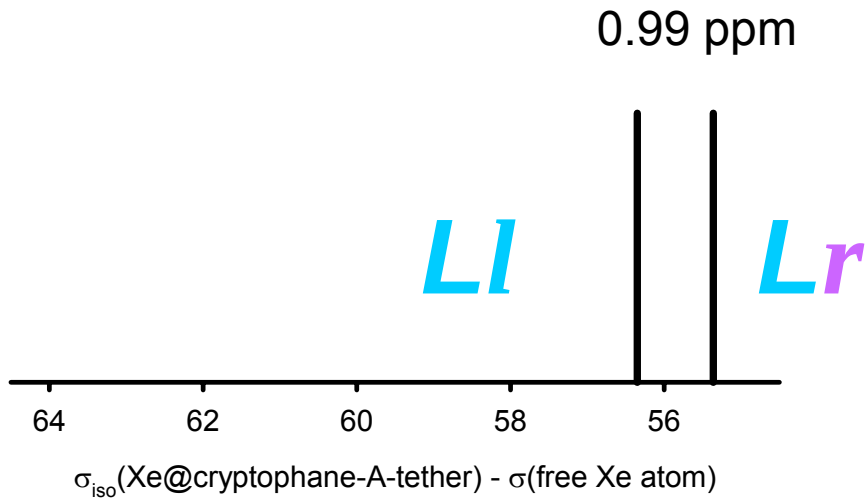
(L)-cryptophane-A-(l)-tether





(L)-cryptophane-A-(r)-tether

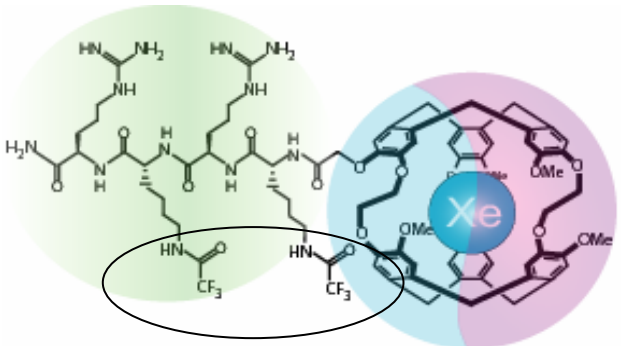
Quantum mechanical Xe shieldings for two spatial configurations of the amino acid tether

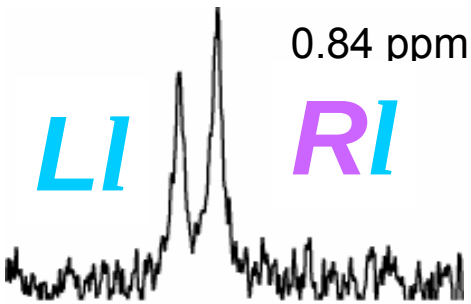


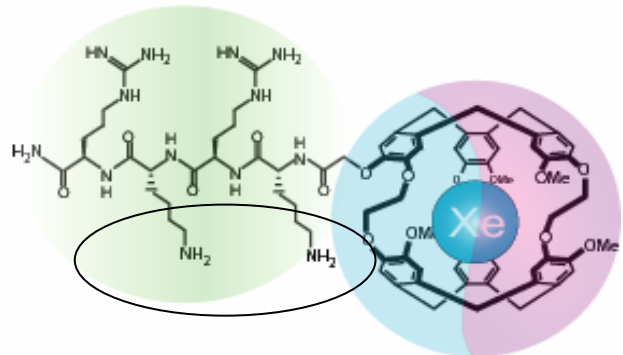
Uniqueness of this assignment is based on systematic studies of the fundamental relations between chirality and the shielding tensor.

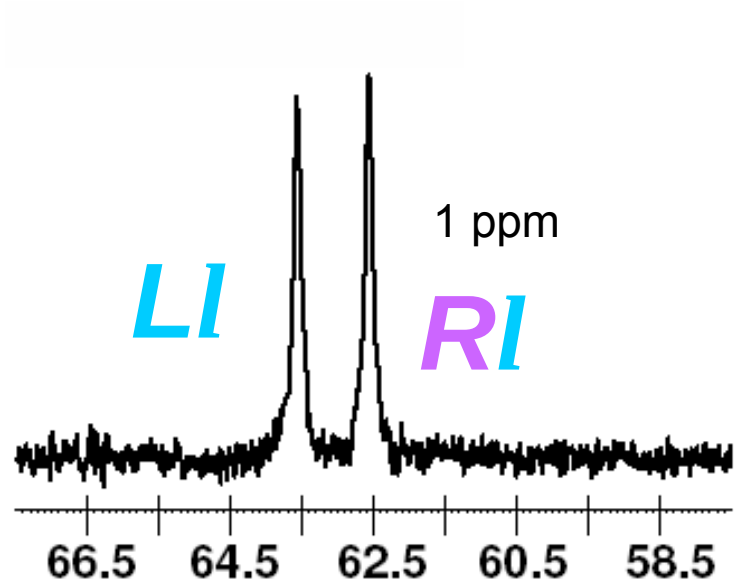
D. N. Sears, C. J. Jameson, R. A. Harris,
J. Chem. Phys, 119, 2685-2701, 120, 3277 (2004)

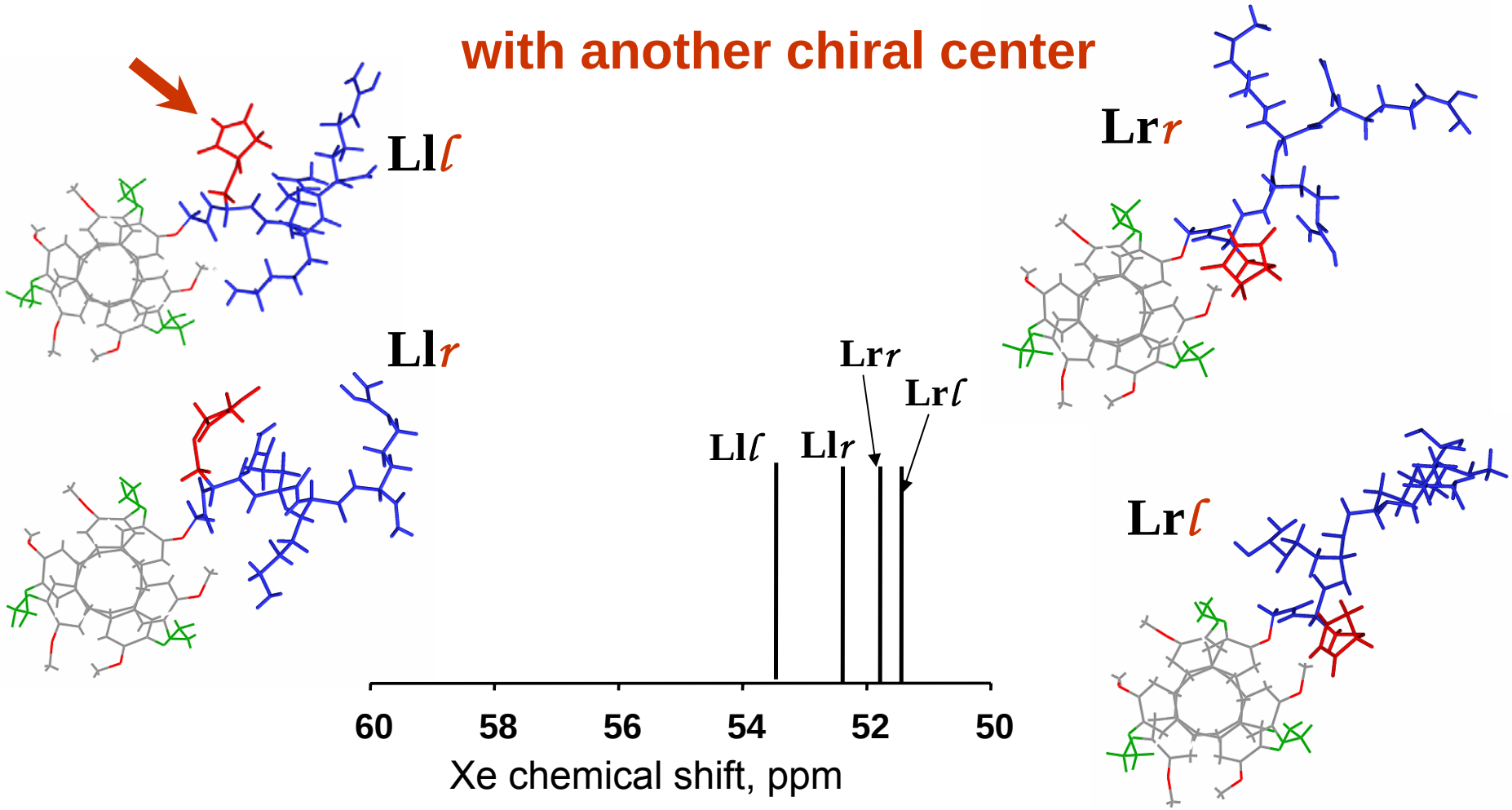
Now we can assign the experimentally observed Xe signals to the specific member of the diastereomeric set





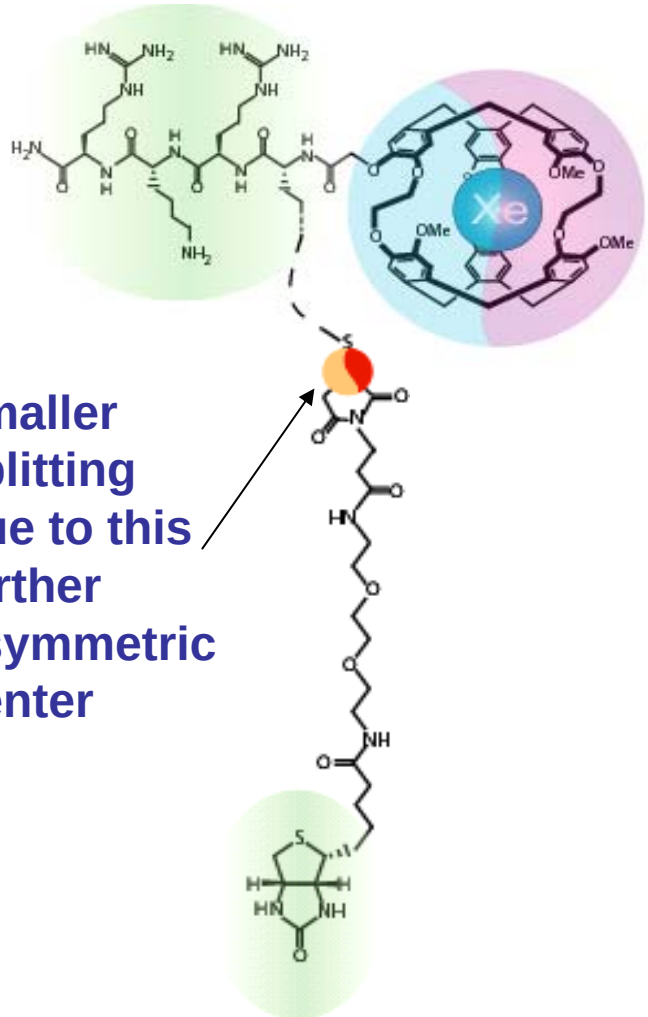




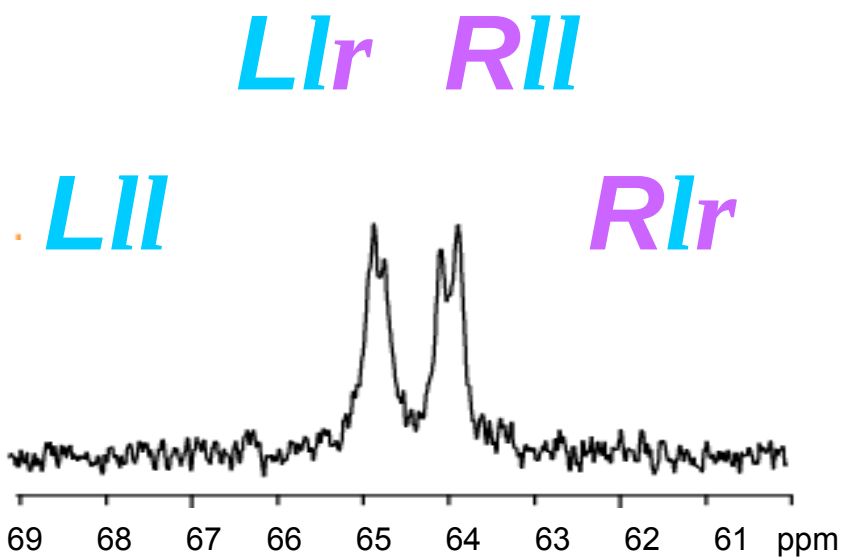


Quantum mechanical Xe shieldings for four spatial configurations of the substituent with respect to the cryptophane-A cage

Now we can assign the experimentally observed Xe signals in the biosensor



smaller splitting due to this farther asymmetric center



CONCLUSIONS

- **Xe embedded in a given chiral molecule is remarkably sensitive to the presence of further chiral systems.**
- **The discrimination is distinct and easily observed: Xe signals in members of diastereomeric sets are split by as much as 1 ppm**
- **Quantum mechanical calculations provide the assignments that could otherwise be obtained only by using enantiotopically pure cryptophane cages.**

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