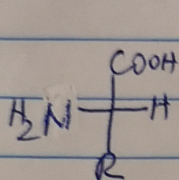


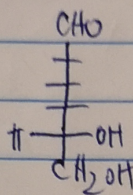
Lecture XXXIV: Origins of Homochirality on Earth

04-23-2020

Probably the biggest unsolved stereochemical mystery. Why are all biomolecules found in just one enantiomeric form:



L-amino acids



D-sugars

The vast majority of all chiral molecules in Nature are found as single enantiomers. But what initially favored one enantiomer over the other?

This question is not only important in biochemistry. All enantioselective catalysis "borrows" chirality from Nature too.

"The Origin of Homochirality" R. Brazil, Chem. World, 2015.

Theories

Astronomical: a meteorite brought L-amino acids to Earth this is convenient, but it simply obscures the question to a different location in space

Evolutionary: both forms existed, but one won over the other or simply "ate" it. Fine, but implies an advanced level of evolution before homochirality originated. No archaeological evidence for it.

Geological: chiral quartz (or other) crystals catalyzed the first



enantioselective reaction, which then got amplified. But where did chiral quartz crystals come from? This question is a bit easier to answer and will talk about it soon.

But maybe quartz instead polarized light and this asymmetric physical stimulus caused enantioselectivity?

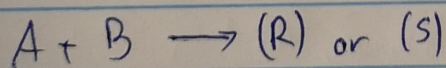
absolute asymmetric synthesis } ACIE, 1999, 38, 3418  
Chem Rev, 1998, 98, 2391

This doesn't work nearly as well as one might think and also needs chromophores. A big hoax in the 1990s were claims that magnetic field spinning direction can influence enantioselectivity:

ACIE, 1994, 33, 1457 - claim proven to be false  
- 1st author stripped of PhD

### Single Event (Flip of a coin)

What if there was a reaction that proceeded only on a small number of molecules? Racemate is a statistical collection:



↳ → → →

50% (R) + 50% (S)

with billions of molecules

But with just a handful, relatively large #s can be temporarily created. They need to be amplified, though!

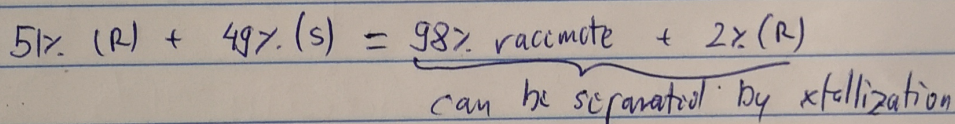


## Chiral Amplification

How do we amplify a miniscule initial ee into a significant amount? There is no general answer to this question yet, but there are very promising methods out there:

- enzymic, but let's ignore them for now, because they imply a higher level of evolution.
- physical amplification through crystallization

Remember that a racemate has different solubility from pure enantiomers? So:



Furthermore, if pure enantiomer is less soluble, it can act as a seed for pulling most of itself away from solution - this is the amplification step! This, or the spontaneous resolution of enantiomers during crystallization could have been the first effects that allowed mass production of an enantiopure material. The same logic applies to the creation of chiral quartz crystals.

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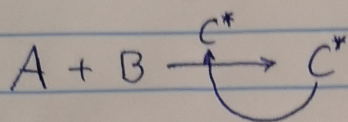
JACS 2008, 130, 1158

-chemical amplification

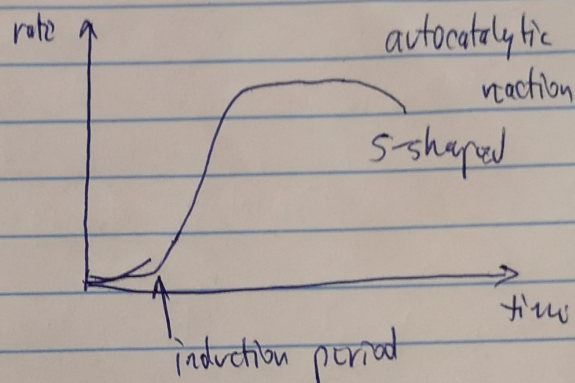
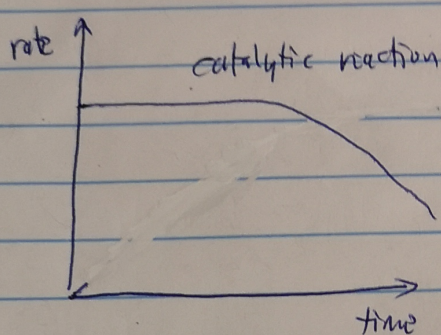
-this is a nonlinear amplification of an ee

↳ simple catalysis will not cut it  
needs to be autocatalytic





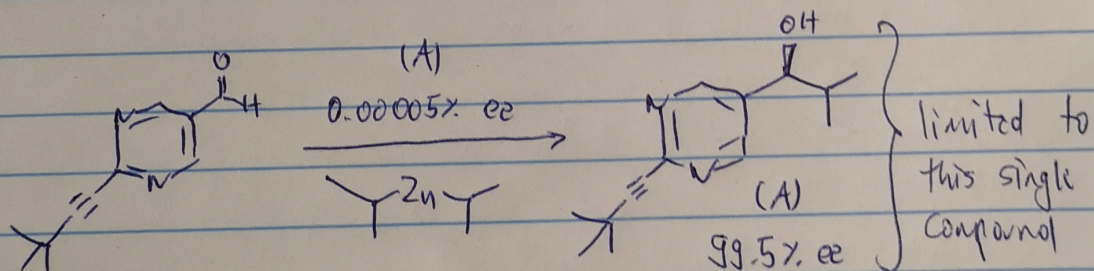
$C^*$  is chiral and a catalyst for its own formation



However, the number of reactions that show this behavior is very small. Soai reaction (1995):

Nature

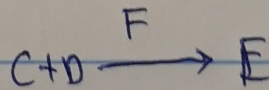
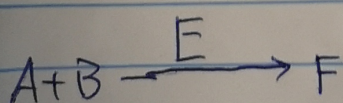
1995, 378, 767



Very small excess of chirality can be amplified, and also chirality of a very subtle kind can be amplified:  $^{13}\text{C}/^{12}\text{C}$ , for example [Soai, Science, 2009, 324, 492]. Chirality can "snowball"...

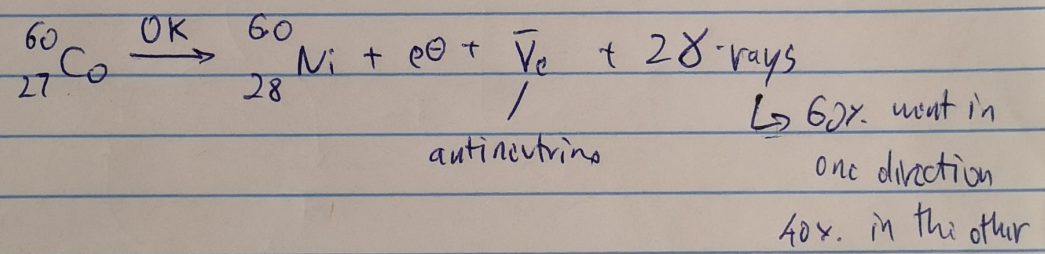
This behavior is exceedingly rare, however!

Autocatalysis may not be the only situation. Cross-catalytic cycles can also work, in which a pair (or more) of molecules amplify each other, without any of them being autocatalytic:



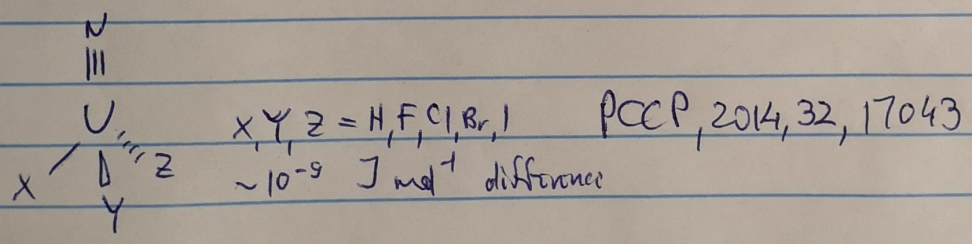


But wait! Are the two enantiomers really equal in energy? For a long time, it was assumed that they must be because of the concept of parity: invariance of physical laws and fundamental forces with the direction in space. However, in 1956, it was observed that parity is violated during radioactive  $\beta$ -decay. Wu experiment:



This difference in direction has little bearing on organic molecules, but can become relevant for heavier molecules:  
ACIE, 2002, 41, 4618

CHFClBr  $\sim 10^{-11}$  J mol<sup>-1</sup> difference



Are these significant? Can they be amplified?

Blackmond Nature Chemistry 2019, 11, 957

Minimal ee that can be amplified:  $3.5 \times 10^{-7} \leftrightarrow 3.5 \times 10^{-8}$

$$\Delta E = 1.5 \times 10^{-10} \leftrightarrow 1.5 \times 10^{-11} \text{ J mol}^{-1}$$