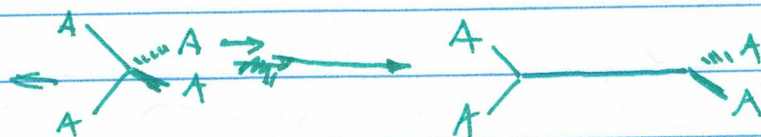


Lecture IX: Axial Chirality

02-03-2020

We have seen that chirality is a geometric concept, and that existence of a single chiral atom can produce it. But there are compounds that are chiral without having chiral centers. Consider taking a tetrahedron and stretching it:



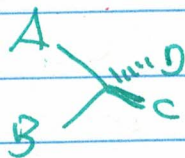
Symmetry group
T

Symmetry group
D_{2d}



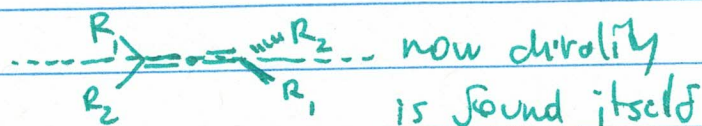
all four substituents need to be different for chirality

only two pairs need to be different because of lower symmetry



but what is this linker chemically

Allenes

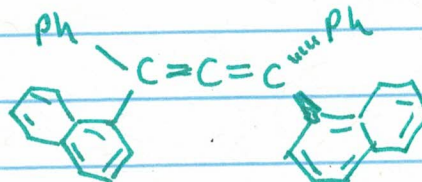
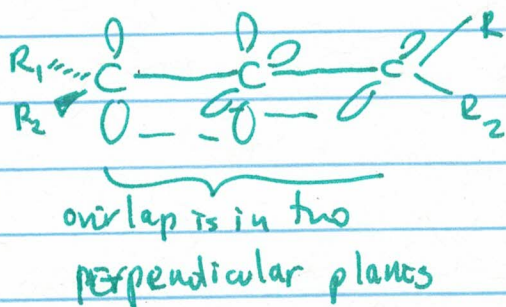


chiral

around an axis = axial chirality!

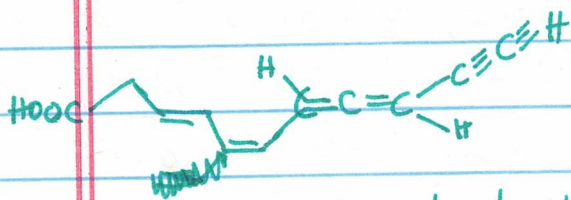
(predicted by van't Hoff 60 yrs before synthesis)

Allene structure is a consequence of orbital geometry:



First chiral allene ever made (1936)
Nature, 1935, 135, 994

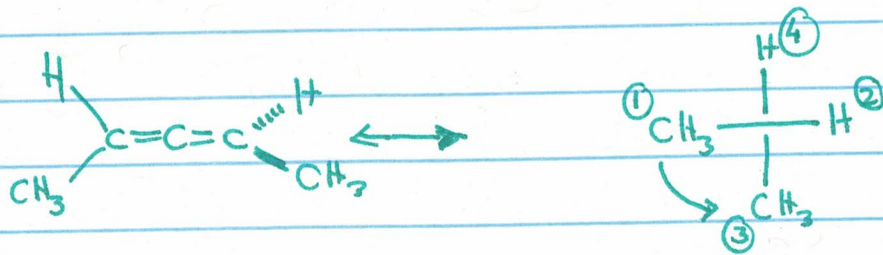
Chiral allenes exist in Nature:



a number of other chiral allenes have been identified

mycomycin - chiral antibiotic (JACS, 1953, 75, 1372)

Naming the enantiomers is no longer R or S:

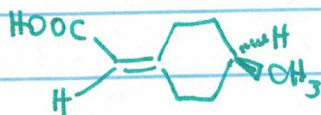
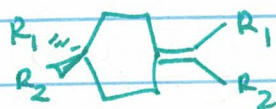


substituents closer to us have higher priorities

If going from ① to ③ is clockwise: P-configuration.
" " " " " " counterclockwise: M-configuration

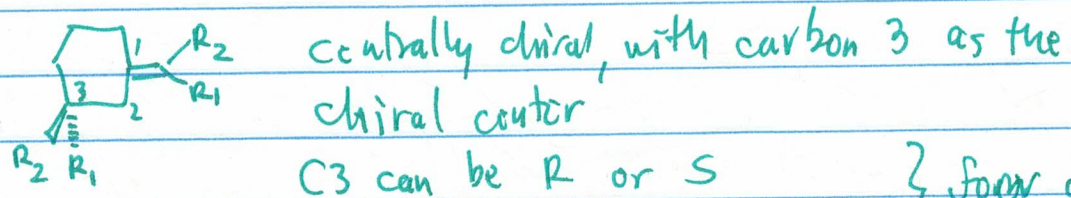
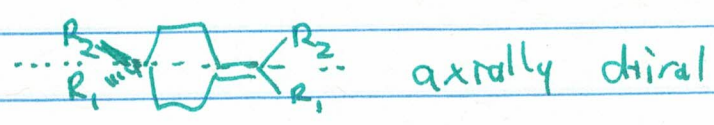
Alkylidene cycloalkanes

Cyclohexane derivatives are the most common:



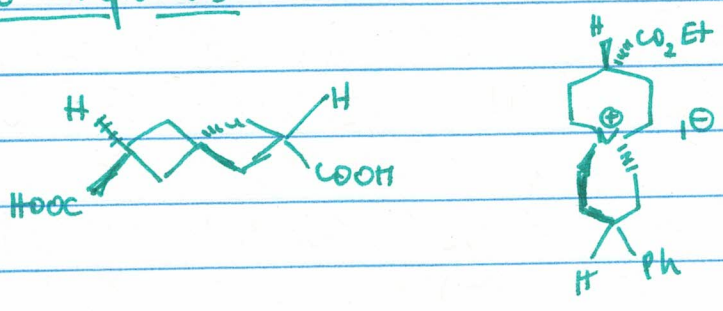
chiral, resolved into enantiomers

Not all isomers are axially chiral

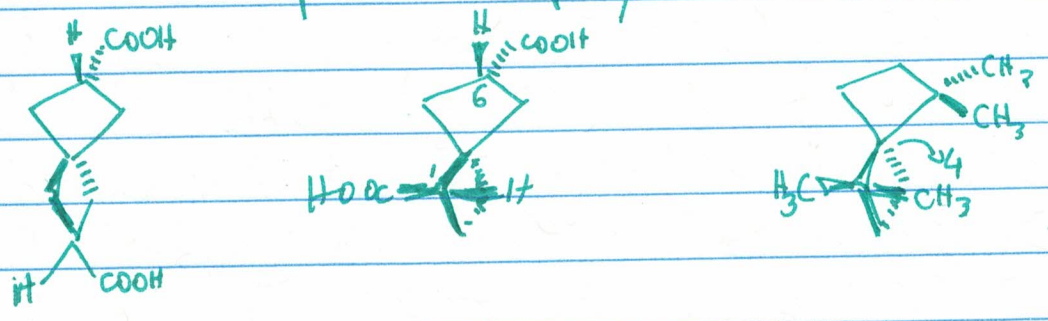


C3 can be R or S
 R1 can be cis or trans to C3 } four diastereomers

Spiro compounds



Just like in the previous example, there are nuances with isomers



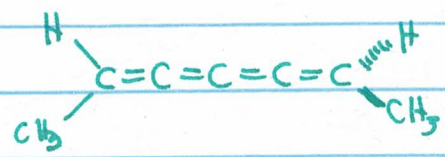
axially chiral
 two enantiomers

Centrally chiral
 C1 is a chiral center; C6 can be cis or trans
 four stereoisomers

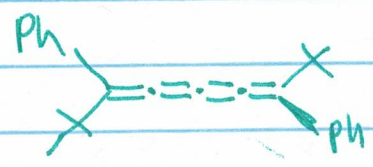
axially chiral
 but C4 can also be treated as a chiral center

Allene analogs

Compounds with an even number of cumulative double bonds should all behave like allenes:

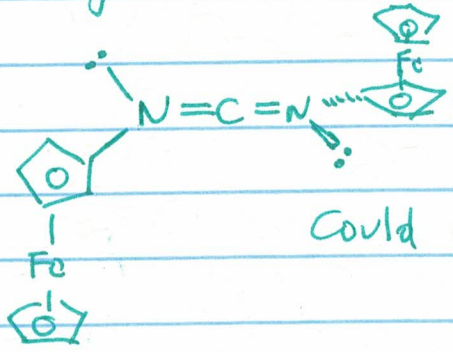


However, barrier for rotation decreases with an increasing number of double bonds, so isolating the enantiomers gets tricky



Isolated as enantiomers only in 1977 (TL, 1977, 4379) unstable, racemizes @ -15°C in a couple of hours

Nitrogen derivatives of allenes occasionally can be separated too:



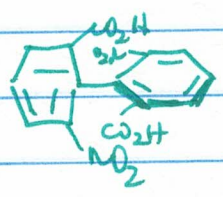
Could be separated into enantiomers.

All of these examples are configurationally enantiomeric.

Diphenyls

These are the most significant examples of compounds in which enantiomers result from conformational effect: restricted rotation around a C-C single bond. These isomers are called

atropisomers (a=not; tropos=turn)



first isolated in 1922

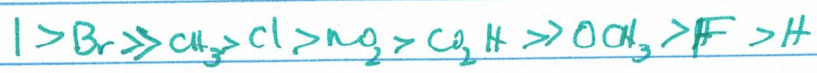
But how slow does this rotation need to be? Oki arbitrarily said that atropisomers exist if they can be isolated and have a half-life of 1000s (~16 min) @ whichever temperature you are studying them:

Ea for inversion: ~22.3 $\frac{\text{kcal}}{\text{mol}}$ @ 300K ~14.7 $\frac{\text{kcal}}{\text{mol}}$ @ 200K

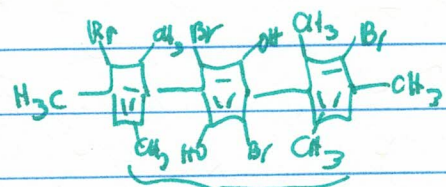
Are all biaryls conformationally restricted:

- If tetrasubstituted, yes, unless two or more groups are F or OCH₃
- If trisubstituted, yes, unless one group is " " "
- If disubstituted, only with large groups such as binaphthyl
- If monosubstituted, no

Substituent sizes influence racemization barrier:



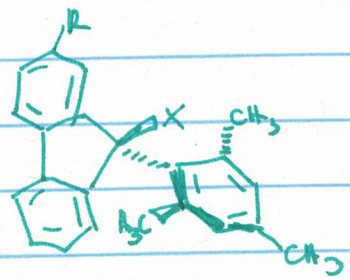
Terphenyls also have isomers:



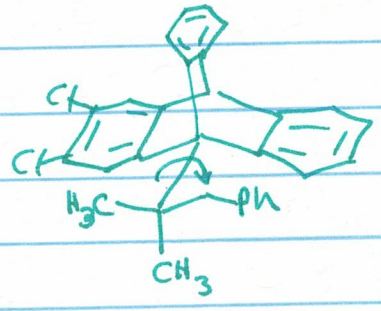
cis methyl groups, could also be trans-

Atropisomerism around the $C(sp^2)-C(sp^3)$ bonds has been the most studied and applied, but it can also be observed around $C(sp^3)-C(sp^2)$ and $C(sp^3)-C(sp^3)$ bonds:

Chem Rev
2015, 115, 11235



mostly fluorinated $C(sp^3)-C(sp^2)$
barriers $\sim 10-20$ kcal/mol



triptycene nucleus in the neighborhood of
a tertiary carbon atom
 $C(sp^3)-C(sp^3)$

Not too many examples of inorganic complexes showing this behavior, even though in principle they should be possible in e.g. trinuclear complexes.