



Kryptoracemates!

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SST44 – Bangkok, 2018

The SunU Connection



*"dans les champs de l'observation, le hasard ne favorise
que les esprits préparés"*

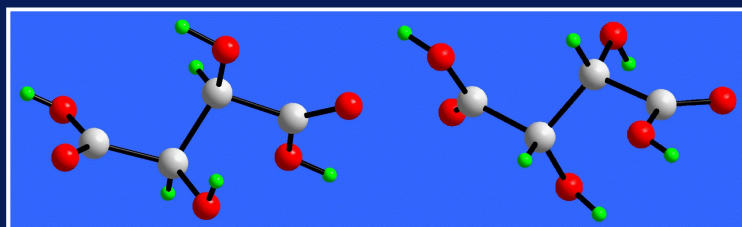
*"In the field of observation, chance favours
only the prepared mind"*

Fortuna Eruditis Favet

"Fortune favours the prepared mind"

Wikipedia

Spontaneous Resolution



L-(+)-tartaric acid

D-(-)-tartaric acid

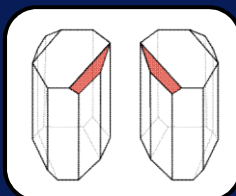
Racemic

Crystallises in $P2_1$!

Physical
mixture

Wikipedia

50%



50%

Conglomerate
Homo chiral
crystals
Spontaneous
resolution

Spontaneous Resolution

Comparatively rare..."not very frequent"^a

90% of crystals crystallise in centrosymmetric
space groups

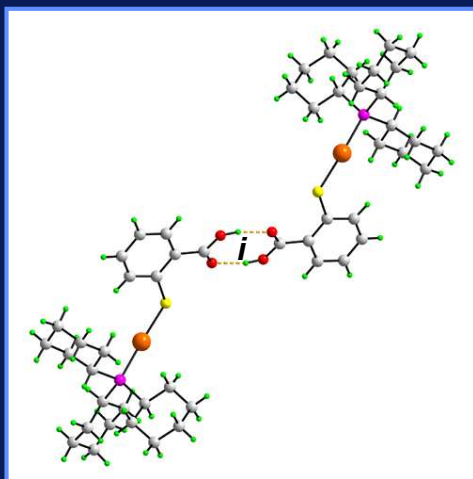
Molecules which can, will crystallise around a centre of
Inversion

Why enantiophobic^b behaviour?

^a Pérez-García & Amabilino, *Chem. Soc. Rev.* 2002, 31, 342

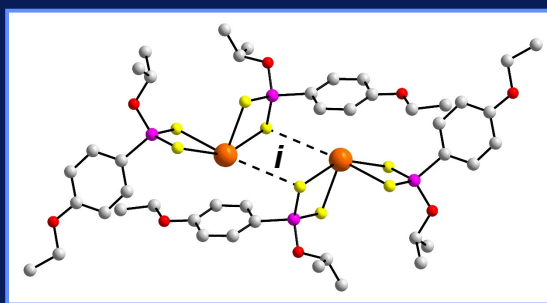
^b Pérez-García & Amabilino, *Chem. Soc. Rev.* 2007, 36, 941

Association about a centre of inversion



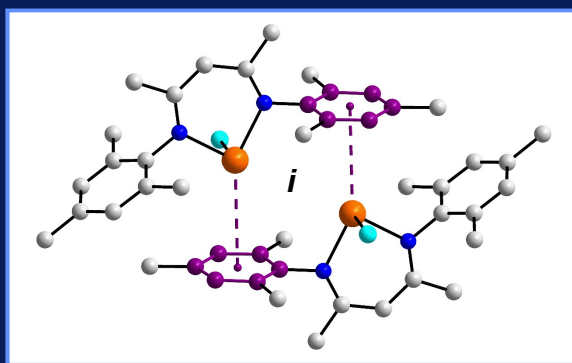
Hydrogen bonding

Association about a centre of inversion



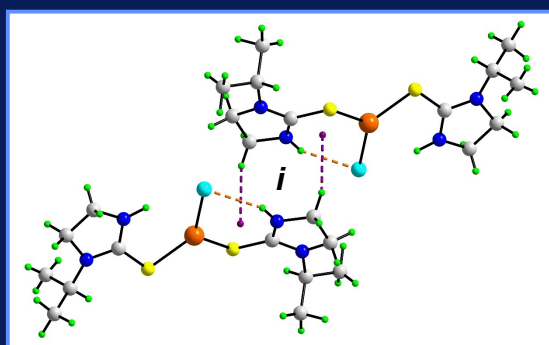
Pb...S secondary (tetrel) interactions

Association about a centre of inversion



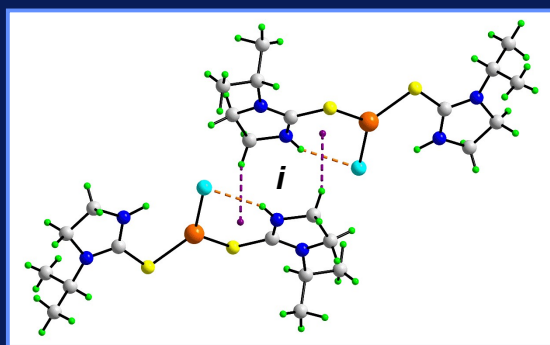
Sn(lone-pair)··· π (aryl) interactions

Association about a centre of inversion



C-H··· π (quasi chelate ring) interactions

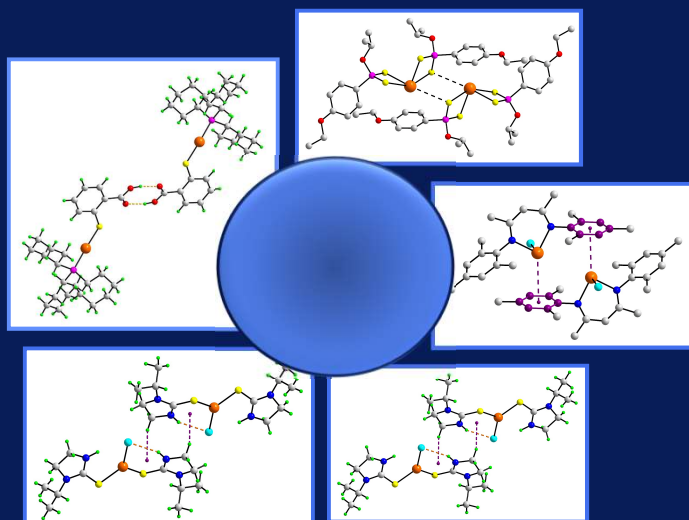
Association about a centre of inversion



WHY?

C-H... π (quasi chelate ring) interactions

Global(ur) Molecular Packing?



The two-molecule aggregates are more spherical

Prevalence of Space Group Adoption

230 Space Groups

CSD: 807,190 entries

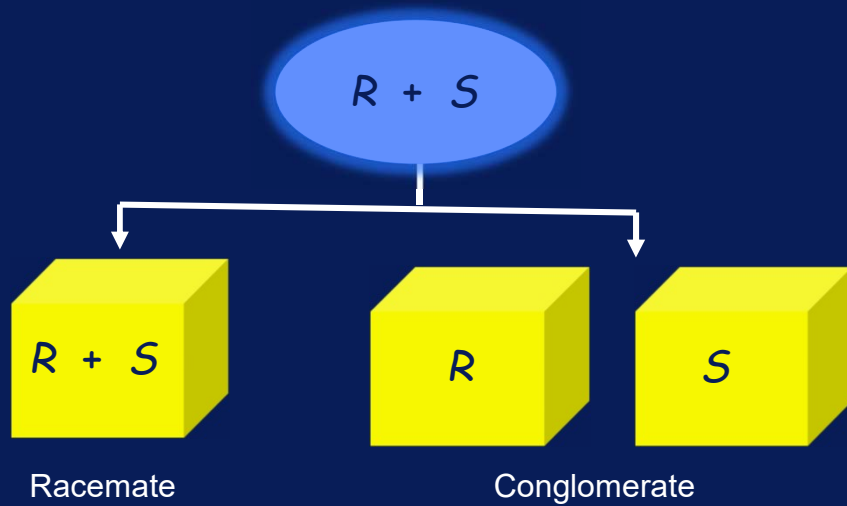
$P2_1/c$	279041	34.6
$P\bar{1}$	198014	24.5
$C2/c$	67434	8.4
$P2_12_12_1$	58438	7.2
$P2_1$	41791	5.2
$Pbca$	26951	3.3

Prevalence of Space Group Adoption

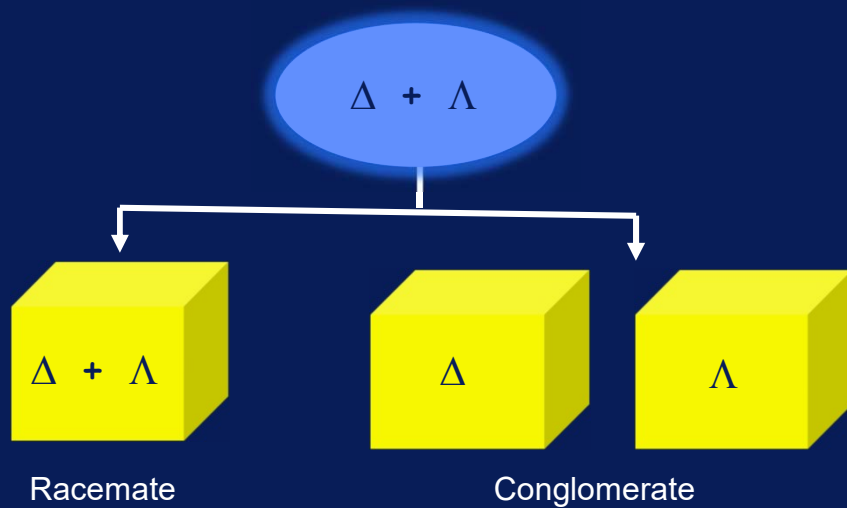
Six Space Groups account for >83% of structures

All are **close-packing** - minimising free-space

Crystallisation outcomes from a racemic solution



Crystallisation outcomes from a racemic solution



Crystallisation outcomes from a racemic solution

For **organics**, racemic compounds, molecules with meso symmetry and achiral molecules will crystallise about a centre of inversion:

99.9%

Today: 0.01% The Kryptoracemates

Prevalence of Space Group Adoption

For organics,

racemic compounds, molecules with meso symmetry and achiral molecules will crystallise about a centre of inversion:

99.9%

Kryptoracemates:

0.1%



Carol Brock

Prevalence of Space Group Adoption



Leonhard Sohncke
(1842–1897)

https://en.wikipedia.org/wiki/Leonhard_Sohncke

Racemic; crystallise in a Sohncke Space Group; $Z' > 1$

Sohncke: 65
{no inversion centre, rotatory inversion axes, glide planes or mirror planes} - for chiral molecules

Kryptoracemates

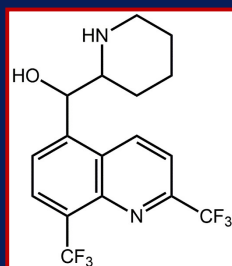
Racemic

Crystallise in a Sohncke Space Group

$Z' > 1$

Pseudo centrosymmetric relationship

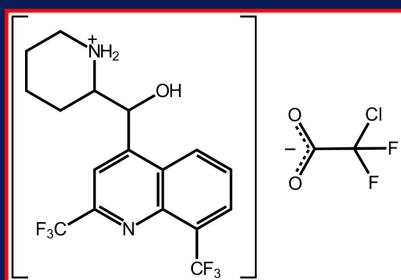
Mefloquine (Mef)



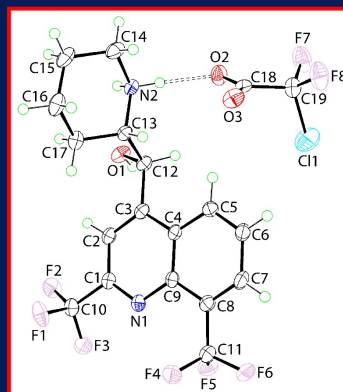
[2,8-bis(trifluoromethyl)quinolin-5-yl](piperidin-2-yl)methanol

Salt formation

1:1 Recrystallisation of $[\pm\text{Mef}] + \text{F}_2\text{ClCCO}_2\text{H}$:

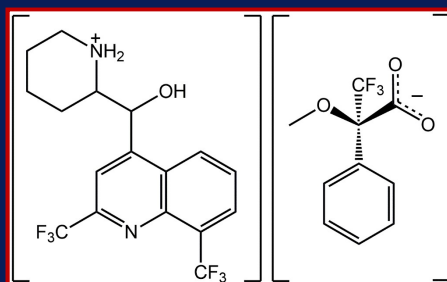


$P2_1/c$



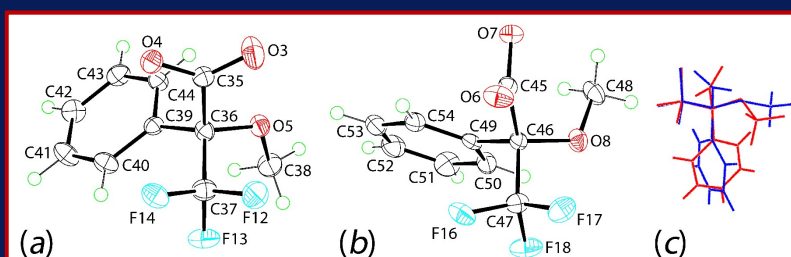
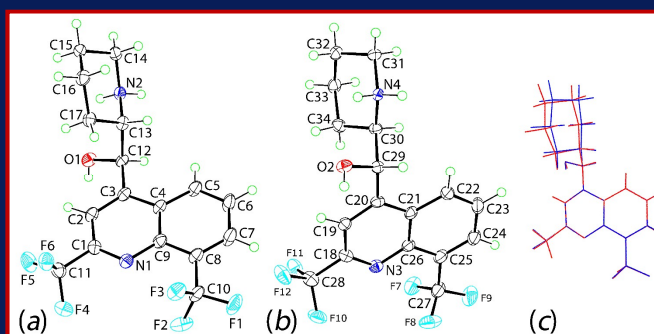
Two kryptoracemates - case 1

1:1 Recrystallisation of [\pm Mef] with a chiral acid:



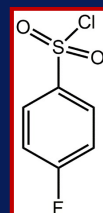
Chiral resolution

Two kryptoracemates - case 1

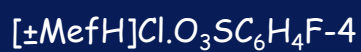


Two kryptoracemates - case 2

1:1 Recrystallisation of $[\pm\text{MefH}]\text{Cl}$ with
in the presence of NaOH

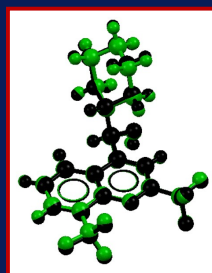
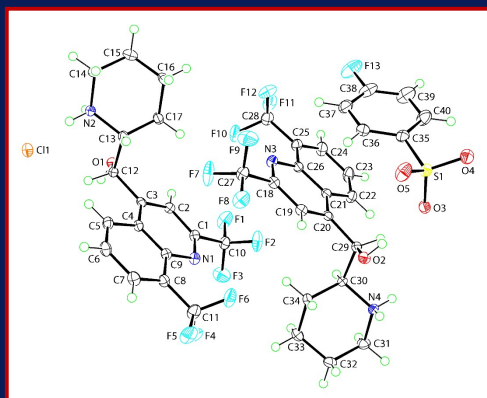


yielded



Anion exchange

Two kryptoracemates - case 2

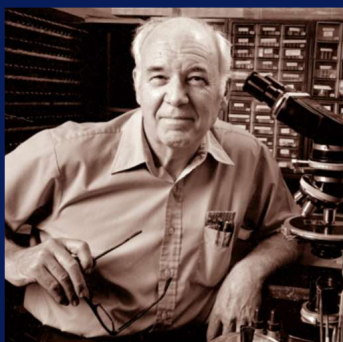


Mediated by different anions/crystal packing

Kryptoracemates

All-organic structures: 0.1%

"Mef" crystals: 2/30!



Dr W. C. McCrone (2016-2002)

"...every compound has different polymorphic forms, and that, in general, the number of forms known for a given compound is proportional to the time and money spent in research on that compound."

<http://mcri.org/>



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Fortuna Eruditis Favet ("*Fortune favours the prepared mind*")