Absolute Configuration

- Types of space groups
- Non-centrosymmetric
- Determining Absolute Configuration

Centric Space Groups

- Any space group that has the inversion symmetry operation
- In this case the phase problem reduces to a determination of the sign of the amplitude.
- Do not need to worry about cell handedness or absolute configuration.

Non-centrosymmetric Space Groups

- Come in two forms.
- Type one is a cell that does not contain an inversion center but does contain a mirror (glide plane) or improper rotation axes. This class of cells can NOT contain enantiomorphically pure compoumds
- The other type does not contain the above symmetry elements and can crystallize optically pure materials—Polar Space Groups

How can a cell be enantiomorphic if the contents are racemic?

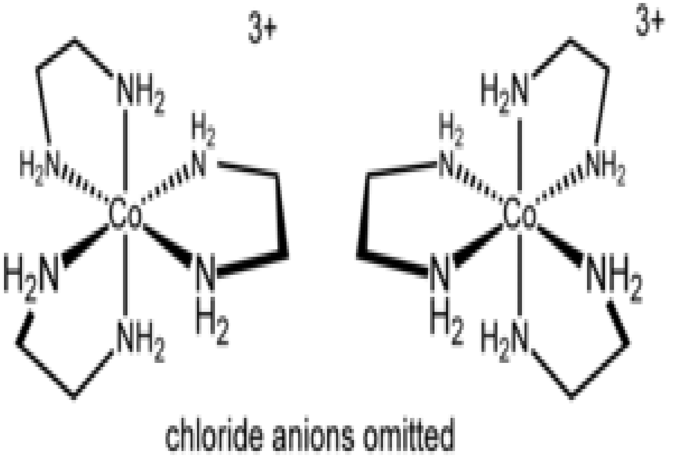
- For non-polar accentric cells the contents are racemic yet the unit cell is enanitomorphic.
- The arrangement of molecules in the unit cell creates the optical activity.
- Is there a chemical analogy?

Consider $Co(en)_3^{3+}$

- Obviously Co^{3+} nor ethylenediamine is optically active

$Co(en)_3$

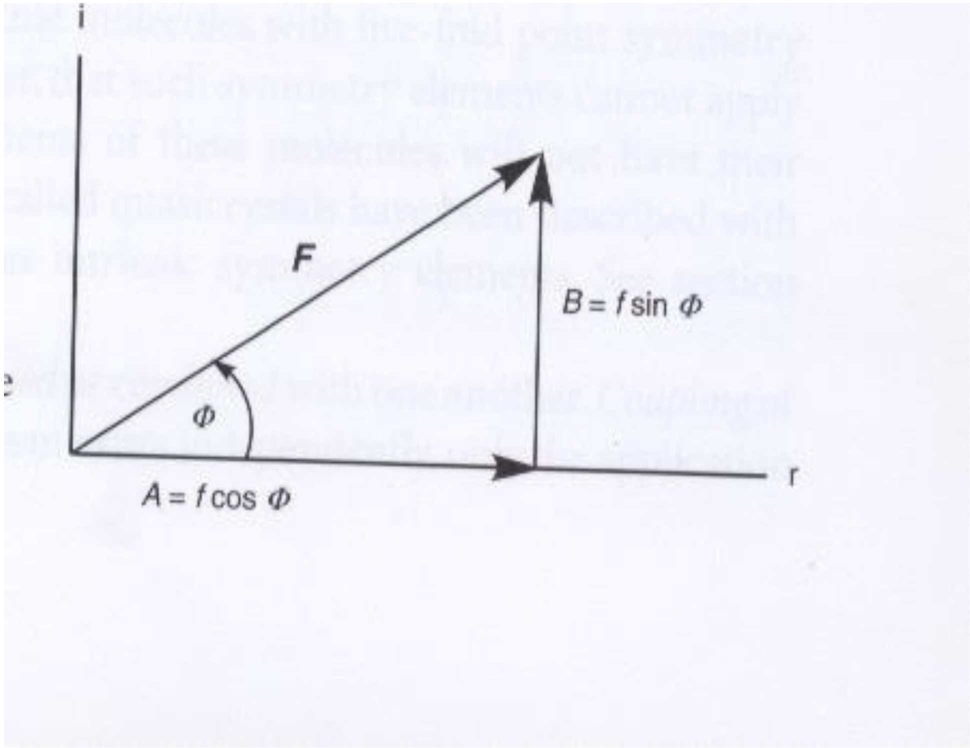
- Yet the ion is optically active
- Note there is not a single enantiomorphic atom in the structure. The overall arrangement creates the optical activity.



Anomalous Scattering(AS)

- AS arises from absorbed then emitted photons.
- These photons are out of phase with the normally scattered photons.
- AS is important in both centric and accentric space groups.
- The components of AS are given by f' and f” where f' is the real and f” the imaginary component.
- The values of f' and f” are functions of the wavelength used but are independent of the scattering angle.

What does imaginary mean?



How does AO effect centric scattering

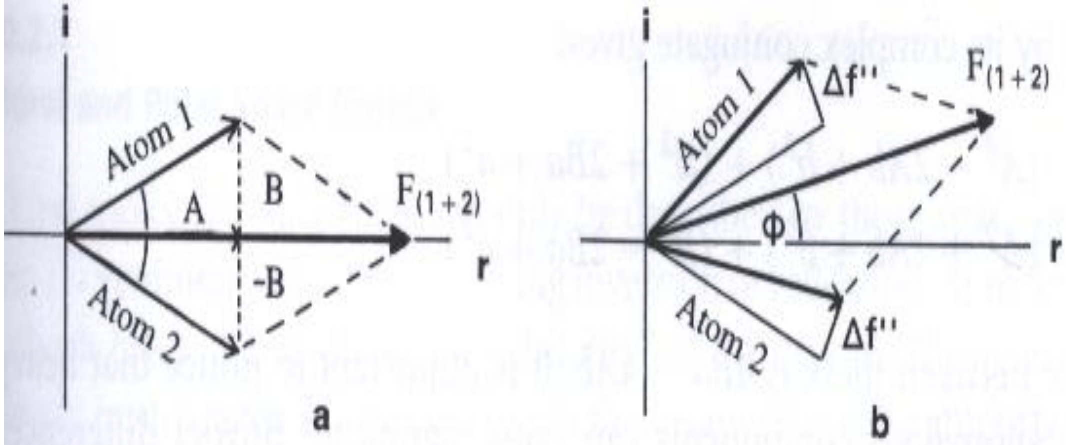


Fig. 10.5. Structure factors for a pair of atoms related by an inversion center (Atom 1 x, y, z; Atom 2 $\bar{x}, \bar{y}, \bar{z}$). **a** without **b** with anomalous dispersion.

How does it effect accentric space groups?

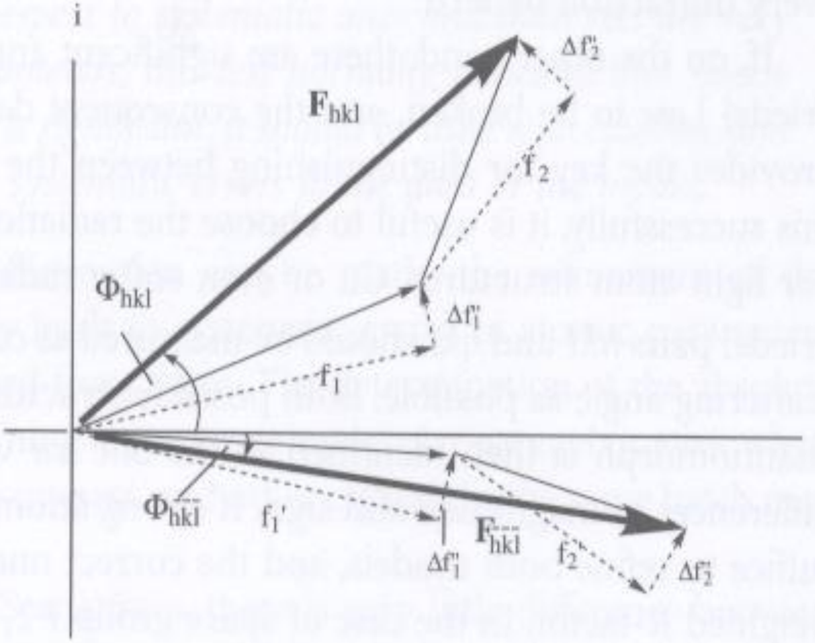


Fig. 10.6. The result of anomalous dispersion in a non-centrosymmetric space group.

A problem

- Since we cannot tell x,y,z from -x,-y,-z then we are not sure which is really hkl and which

  -h-k-l (These are the Friedel pairs)

- This means we do not know if we are adding or subtracting the AS imaginary component from the real component.
- If the handedness is correct and the enantiomorph correct then the addition sign will be correct. If one of these is incorrect then the result will be subtraction.

- If the absolute configuration is correct than the correct Friedel pair will have the correct intensity difference.
- If incorrect than the more intense will actually be less intense and vice versa.
- This is the origin for using AO to determine absolute confguration.
- Discovered by the Dutch crystallographer Johannes Bijvoet.

How big is this effect.

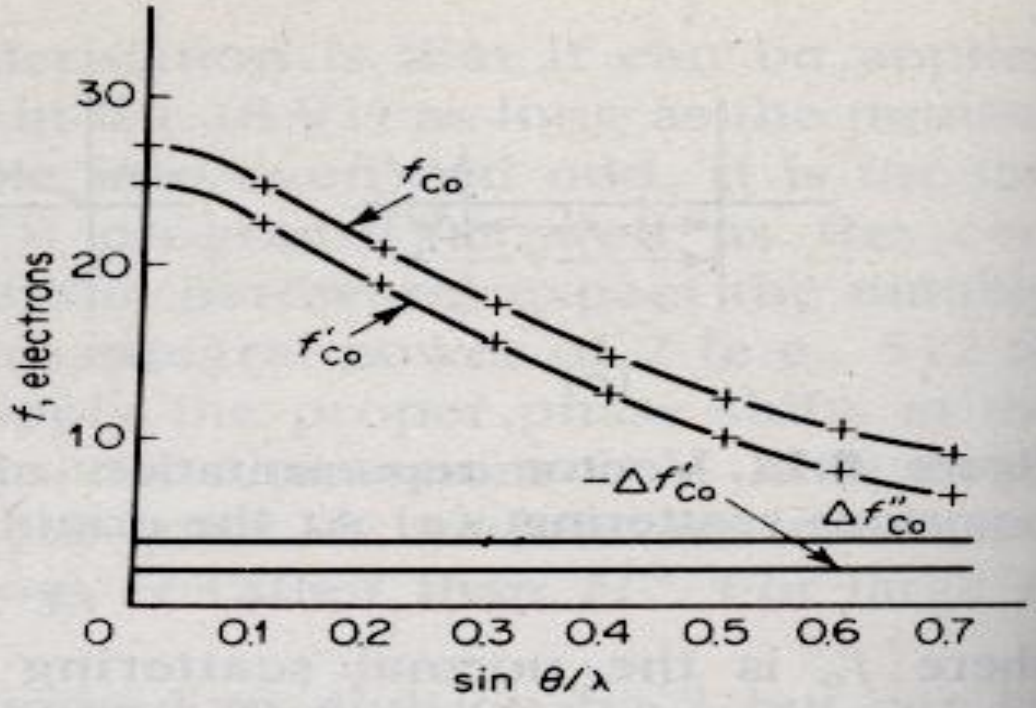


Figure 8.13. f_{Co}, f'_{Co}, $-\Delta f'_{Co}$, and $\Delta f''_{Co}$ for Cu K_α radiation as functions of $(\sin\theta)/\lambda$.

Table 10.1. Anomalous dispersion factors $\Delta f'$ and $\Delta f''$ and mass absorption coefficients μ/ϱ for Cu- and Mo-K_α radiation and a selection of common types of atoms. From *Int. Tab. C* [12] Tables 4.2.6.8 and 4.2.4.3.

	CuK_α			MoK_α		
	$\Delta f'$	$\Delta f''$	μ/ϱ [cm^2/g]	$\Delta f'$	$\Delta f''$	μ/ϱ [cm^2/g]
C	0.0181	0.0091	4.51	0.0033	0.0016	0.576
N	0.0311	0.0180	7.44	0.0061	0.0033	0.845
O	0.0492	0.0322	11.5	0.0106	0.0060	1.22
F	0.0727	0.0534	15.8	0.0171	0.0103	1.63
Na	0.1353	0.1239	29.7	0.0362	0.0249	3.03
Si	0.2541	0.3302	63.7	0.0817	0.0704	6.64
P	0.2955	0.4335	75.5	0.1023	0.0942	7.97
S	0.3331	0.5567	93.3	0.1246	0.1234	9.99
Cl	0.3639	0.7018	106.	0.1484	0.1585	11.5
Cr	−0.1635	2.4439	247.	0.3209	0.6236	29.9
Mn	−0.5299	2.8052	270.	0.3368	0.7283	33.1
Fe	−1.1336	3.1974	302.	0.3463	0.8444	37.6
Co	−2.3653	3.6143	321.	0.3494	0.9721	41.0
Ni	−3.0029	0.5091	48.8	0.3393	1.1124	46.9
Cu	−1.9646	0.5888	51.8	0.3201	1.2651	49.1
As	−0.9300	1.0051	74.7	0.0499	2.0058	66.1
Br	−0.6763	1.2805	89.0	−0.2901	2.4595	75.6
Mo	−0.0483	2.7339	154.	−1.6832	0.6857	18.8
Sn	0.0259	5.4591	247.	−0.6537	1.4246	31.0
Sb	−0.0562	5.8946	259.	−0.5866	1.5461	32.7
I	−0.3257	6.8362	288.	−0.4742	1.8119	36.7
W	−5.4734	5.5774	168.	−0.8490	6.8722	93.8
Pt	−4.5932	6.9264	188.	−1.7033	8.3905	107.
Bi	−4.0111	8.9310	244.	−4.1077	10.2566	126.

Observations

- Because the normal scattering falls off with the diffraction angle but the anomalous scattering does not the AS contribution will be greatest for high angle reflections.
- However, these are the weakest reflections with the largest errors. Means the differences because of AS may be less than the error.
- In general it is impossible to determine the absolute configuration for compounds containing only light atoms (<Na) using Mo radiation
- The heavy atom can be anywhere in the cell.

Changing Absolute Configuration

- Change all atomic positions so xyz is now
- -x-y-z
- Some polar space groups come in pairs
  - $P3_1$ $P3_2$ $P4_1$ $P4_3$ $P6_1$ $P6_5$
  - In this case besides the atomic positions, the space group must be changed to the other of the pair
- For space groups with d glides it is somewhat more complex.

How to determine the absolute configuration

- It must be noted that the configuration is either all correct or all incorrect everywhere.
- Therefore if the configuration of one atom is known it can be used to set all the other atoms.
- Examples
  - Steroids
  - Tartrates using natural tartaric acid
  - Part of a molecule unchanged in synthesis.

Bijvoet Method

- Collect all data and Friedel pairs.
- Find the pairs that have the biggest intensity difference between hkl and -h-k-l
- See how these agree with Fcalc
- Change the absolute structure and see if the agreement improves or gets worse.
- Problem: need twice as much data as needed to solve the structure

R-factor method

- Refine one absolute structure to completion
- Invert the structure and refine this to completion.
- Compare the R-factors.
- The lowest one is correct. However, need to do a statistical analysis using Hamilton's T test to determine if this is statistically real.
- Advantage—do not need Friedel pairs
- Disadvantage – usually fails unless there is a heavy atom present.

Refinement Parameters

- Rogers suggested refining the sign of the anomalous terms. +1 means correct -1 means incorrect. While this works the parameter is very slow to converge and requires many cycles of refinement before it settles down.
- Howard Flack suggested use a parameter to refine both enantiomers at once. The one being refined had an occupancy of (1-x) while the other was x.
-

Flack Parameter

- If the Flack Parameter (x) refines to zero then the enantiomer is correct, while 1 is incorrect.
- The Flack Parameter can take on values outside of 0 to 1. These are generally meaningless and suggest the anomalous scattering is too weak to use.
- The s.u. in the Flack Parameter is important.
  - 0.2(1) suggests correct.
  - 0.2 (6) suggests nothing.

Flack Parameter

- Advantages
  - Do not need Friedel pairs to calculate.
  - Provides a quantitative indicator of the absolute configuration.
- Disadvantages
  - The Flack Parameter tends to correlate with other parameters when there is not much Friedel pair data.
  - It is not Chemist friendly

The Hooft Approach

- Rob Hooft and Ton Spek worked on a new approach.
- They assumed that most of the Friedel data would be collected which is true for modern area detectors.
- Their method is in PLATON as the Bijvoet calculation and appears in our table ent.txt

Good Output

```
              Absolute Structure Analysis


   Flack Parameter                          0.050 +/- 0.060

   Hooft Parameter                          0.024 +/- 0.037

   Friedel Coverage                              99.6%

  Assuming No Racemic Twinning is Present
   Probability Absolute Structure is Correct       1.000

   Probabilities Allowing for Racemic Twinning
   Probability Absolute Structure is Correct       1.000
   Probability Absolute Structure is Incorrect     0.0E+00
   Probability Crystal is a Racemic Twin          0.2E-35
```

Hooft,R.W.W.,Straver,L.H.,and Spek, A.L.(2008). J. Appl. Cryst.,41,96-103.

Undetermined Output

```
                    Absolute Structure Analysis


          Flack Parameter                                  0.400 +/- 1.200

          Hooft Parameter                                  0.417 +/- 0.634

          Friedel Coverage                                      98.6%

         Assuming No Racemic Twinning is Present
          Probability Absolute Structure is Correct       0.551

          Probabilities Allowing for Racemic Twinning
          Probability Absolute Structure is Correct       0.329
          Probability Absolute Structure is Incorrect     0.267
          Probability Crystal is a Racemic Twin           0.404
          The absoloute structure could be better determined by
          collecting another data set using copper radiation!
```

Hooft,R.W.W.,Straver,L.H.,and Spek, A.L.(2008). J. Appl. Cryst.,41,96-103.

Borderline

```
              Absolute Structure Analysis


Flack Parameter                          0.210 +/- 0.180

Hooft Parameter                          0.216 +/- 0.070

Friedel Coverage                              94.6

Assuming No Racemic Twinning is Present
Probability Absolute Structure is Correct       n/a

Probabilities Allowing for Racemic Twinning
Probability Absolute Structure is Correct       0.970
Probability Absolute Structure is Incorrect     0.8E-25
Probability Crystal is a Racemic Twin          0.030
```

Borderline

Absolute Structure Analysis

Flack Parameter	0.210 +/- 0.180
Hooft Parameter	0.216 +/- 0.070
Friedel Coverage	94.6

Assuming No Racemic Twinning is Present

Probability Absolute Structure is Correct	n/a

Probabilities Allowing for Racemic Twinning

Probability Absolute Structure is Correct	0.970
Probability Absolute Structure is Incorrect	0.8E-25
Probability Crystal is a Racemic Twin	0.030

Hooft Method

- Advantages
  - Very Quantitative
  - Chemist Friendly
  - Lower errors on the Hooft y Parameter than the Flack Parameter
- Disadvantages
  - Requires Friedel pair data
  - Is very sensitive to how data is collected.