Absolute Configuration Determination using the Anomalous Scattering of Cu-K_α X-Rays by Oxygen Atoms: Cellobiose

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Summary The anomalous scattering effects of oxygen atoms have been measured and their usefulness confirmed by the determination of the absolute configuration of cellobiose.

THE anomalous scattering of X-rays by atoms in molecular crystals has been used for the determination of the absolute configuration of molecules since the pioneering work of Bijvoet.[1] Most of the atoms whose anomalous scattering effects have been so used have been atoms whose f'' values ($f = f' + if''$) are relatively large. The smallest f'' value successfully employed and reported prior to January 1969 was 0·4 for silicon.[2]

We chose the molecule cellobiose, $C_{12}H_{22}O_{11}$, to test the possibility and the effectiveness of measuring and using the anomalous scattering effects of oxygen atoms in a typical organic crystal. The structure of cellobiose is known[3] as is its absolute configuration which has been determined by non-crystallographic techniques.[4]

Values of $\Delta I_{hkl} = I_{hkl} - I_{\bar{h}\bar{k}\bar{l}}$ and $FDEL_{hkl} = 2|\Delta I_{hkl}|/(I_{hkl} + I_{\bar{h}\bar{k}\bar{l}})$ were calculated for the structure as reported by Brown,[3] using $f'' = 0{\cdot}1$ for oxygen with Cu-K_α radiation.[5]

A crystal of cellobiose was grown from ethanol solution and the space group ($P2_1$) and unit-cell dimensions given by Brown[3] were confirmed, the crystal being mounted on the *c* axis. With a manually operated Buerger diffractometer and Cu-K_α radiation intensities were carefully measured for the pairs of reflections which our calculations indicated would have both accurately measurable intensities and calculated *FDEL* values greater than 0·07. Each of these pairs, referred to below as "large Bijvoet pairs," was measured at least four times.

The crystal was rather irregular in shape and too brittle to cut or grind into a shape for which absorption corrections could be accurately calculated. An empirical approach for determining the absorption corrections was developed. All pairs of reflections whose calculated *FDEL* values were less than 0·02 and for which the θ, ϕ, and μ angles of one reflection were each less than 15° different from the corresponding angles of one member of a large Bijvoet pair and for which the θ, ϕ, and μ angles of the other reflection were also less than 15° from the angles of the second member of the large Bijvoet pair were recorded at least four times. The ratio of the observed intensities was calculated for each pair. The absorption correction factor applied for a large Bijvoet pair was the average of all the intensity ratios for pairs related as above to that particular large Bijvoet pair.

After absorption corrections were applied the signs of the measured values for ΔI_{hkl} were compared with the signs of the corresponding calculated ΔI_{hkl} values. The results are given in the Table. The average of the observed *FDEL* values for the eighteen pairs is 0·054 with a range of 0·023 to 0·135. The values measured were in general somewhat lower than those calculated, due to the use of a value of f'' for oxygen which is too large. The use of $f'' =$ 0·05 produces approximate agreement. (Hönl[6] calculated a value of 0·04 while Zachariasen[7] obtained an empirical value of 0·028.)

A comparison of the signs of the observed and calculated ΔI_{hkl} *values for those pairs of reflections for which the calculated* FDEL *was greater than* 0·07, *the observed* FDEL *greater than* 0·02, *and the average calculated* I_{hkl} *greater than* 1·0.

	Sign of observed ΔI_{hkl}		
$hkl/\bar{h}\bar{k}\bar{l}$	Without absorption correction	With absorption correction	Sign of calculated ΔI_{hkl}
$120/\bar{1}\bar{2}0$	−	−	−
$\bar{1}20/\bar{1}\bar{2}0$	−	−	−
$\bar{1}20/1\bar{2}0$	+	−	−
$130/\bar{1}\bar{3}0$	−	−	−
$\bar{1}30/\bar{1}\bar{3}0$	−	−	−
$130/1\bar{3}0$	+	−	−
$\bar{1}30/1\bar{3}0$	+	−	−
$\bar{6}40/\bar{6}\bar{4}0$	−	+	+
$640/6\bar{4}0$	+	+	+
$\bar{6}40/6\bar{4}0$	+	+	+
$221/2\bar{2}1$	+	+	+
$\bar{3}21/\bar{3}\bar{2}1$	−	−	−
$\bar{4}31/\bar{4}\bar{3}1$	−	−	−
$\bar{2}22/\bar{2}\bar{2}2$	−	−	−
$\bar{1}42/\bar{1}\bar{4}2$	+	+	+
$\bar{1}22/\bar{1}\bar{2}2$	+	+	+
$\bar{2}52/\bar{2}\bar{5}2$	−	−	−
$053/0\bar{5}3$	+	−	−

For the space group $P2_1$ $I_{hkl} = I_{\bar{h}kl}$ and $I_{\bar{h}\bar{k}l} = I_{\bar{h}\bar{k}\bar{l}} = I_{h\bar{k}l}$.

These results show complete agreement between the calculated and corrected observed signs. The correct absolute configuration must then be that configuration given by Brown.[3] Since this is the absolute configuration given by other methods,[4] these results clearly demonstrate that the effects of the anomalous scattering of Cu-K_α X-rays by oxygen atoms can be accurately measured and that these effects can be used to determine the correct absolute configuration of molecules. The effectiveness and necessity of the empirical absorption corrections used is also indicated.

During the course of this work Hope and de la Camp[8] published a report in which they discussed the successful determination of the absolute configuration of (+)-tartaric acid using the anomalous scattering of X-rays by oxygen atoms. There are several important differences between their reported work and the present study. The crystals of tartaric acid used were ground into spheres for which absorption corrections are easily calculated. Most organic crystals are too brittle for such a procedure. Also Hope used the R-factor test[9] to decide between the two possible enantiomers instead of the direct measurement of the anomalous scattering effects. We believe the comparison of observed and calculated ΔI_{hkl} values for a reasonable number of intensity pairs is more direct, more practical, and provides clearer proof of the absolute configuration than a small difference in R values for a limited set of data, especially for typical organic crystals.

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