

Note

# Centrosymmetric crystal structures described as non-centrosymmetric: An analysis of reports in *Inorganica Chimica Acta*

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## Abstract

A full set of centrosymmetric crystal structures published in *Inorganica Chimica Acta* as being non-centrosymmetric has been examined. Many have origin-free directions in the non-centrosymmetric description. Frequently insufficient data have been measured. Values obtained for the Flack parameter have been analyzed. With sufficient data coverage, a value close to 0.5 is obtained. With insufficient data a value near to zero has been observed and explained. Many of these structures qualify for the *ORTEP-of-the-Year* prize.

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## 1. Introduction

Clemente [1] has studied the 8466 crystal structures published in *Inorganica Chimica Acta*. For these he proposes 52 space-group changes and discusses their chemical consequences. Clemente's study is based on considerations of molecular and crystal geometry and particularly the apparent inconsistencies in these arising from a wrong choice of space group. Through this work, Clemente is not only setting the scientific record straight but he is also offering a very useful lesson for authors, editors, referees and publishers in the necessities and the standards required for reporting, evaluating and publishing crystal and molecular structure information in a scientific text. To be sure, this crystallographic and reporting problem is by no means specific to *Inorganica Chimica Acta* and needs to be taken very seriously by all concerned.

We have examined the results of Clemente's study from a different viewpoint making a particular concern of the chemical aspects of chirality. As the space group of these

52 "wrong" crystal structures have been assigned incorrectly, it may well be that authors have followed unsatisfactory experimental procedures in measuring and treating the X-ray diffraction data, and that there were signs, other than the molecular and crystal geometry, to indicate that the crystal-structure analysis might be erroneous. Moreover, it is of concern that critical information necessary for the evaluation of the crystal structures may not be available in the papers and supplementary material.

Clemente's results allow us to study in real situations the way in which the value of the Flack parameter [2], used in modelling any non-centrosymmetric crystal structure, behaves when the assumed model is non-centrosymmetric but the real crystal structure is centrosymmetric. The chemical composition of the 52 "wrong" structures discovered by Clemente is particularly propitious as all contain elements giving significant resonant scattering (anomalous dispersion). Under these conditions a non-centrosymmetric crystal structure is capable of displaying a non-centrosymmetric diffraction pattern. Moreover, a good proportion of Clemente's "wrong" structures was measured with modern equipment and has been published over the last ten years by authors and with referees and editors who are still in activity.

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## 2. Data gathering

We selected those 21 structures published after 1995 which Clemente [1] found were better represented as being centrosymmetric than non-centrosymmetric. Referee 2 was most kind to draw our attention to three further structures published in *Inorganica Chimica Acta* but which had already published corrections (HICMUB [3], NALCIM [4], TOSSAV [4]) prior to Clemente's [1] study. Two of these three structures have been published after 1995 and have been selected for inclusion in our study. All of these structures contain chemical elements having significant resonant-scattering effects at the X-ray wavelengths used for the diffraction experiments. As sources of data, we used the papers as published in *Inorganica Chimica Acta* and any supplementary material (available for 16 out of 23 structures) freely available for download from the CIF archive of the Cambridge Crystallographic Data Centre (CCDC) [5]. Each paper was searched for the following strings of characters: ⟨Flack⟩, ⟨absolute⟩, ⟨enantio⟩, ⟨CD⟩, ⟨optical⟩, ⟨chiral⟩ and ⟨racem⟩. Values pertinent to this study are presented in Table 1. A “?” means that the corresponding value was not reported or could not be deduced from the data sources.

- The compounds are identified by their CSD 6-character Refcode and the complete literature reference to each compound may be found in [1,3,4].
- Two aspects of the symmetry of the “wrong” model crystal structure are given in Table 1 in columns S and P. S indicates one of the three two-letter codes for crystal structures [6]: NC non-centrosymmetric chiral crystal structure; NA non-centrosymmetric achiral crystal structure; CA centrosymmetric achiral crystal structure. P indicates the number of directions in which it is NOT possible to fix the origin of the (non-centrosymmetric) space group with respect to a symmetry element. In the rest of this paper, we will call these origin-free directions. This information is available in tables of the Euclidean normalizers of space groups [7].
- The column *Absolute Structure* gives information from the least-squares refinement on the modelling of the absolute structure.  $x$  refers to the Flack parameter [2].
- The column *Friedel coverage* gives a measure of the completeness of the diffraction intensity data with regard to inversion in the origin of reciprocal space. Reflections  $hkl$  and  $-h-k-l$  are called Friedel opposites. If for each value of  $hkl$ , the intensity of the Friedel opposite  $-h-k-l$  (or one symmetry-equivalent to it) has not been

Table 1  
Data and refinement analysis of centrosymmetric structures refined as non-centrosymmetric

Refcode	S	P	Absolute structure	Friedel coverage	Refinement software
NIGKAP	NA	2	?	0	SIR CAOS
TEWPUG	NC	3	?	100	SDP/VAX V 2.2
LAGQEP	NA	2	?	0	XTAL3.2
MUJZAS	NC	3	?	0	XTAL3.4
QARPUU	NC	3	?	0	TEXSAN
ABOSUF	NC	3	?	0	TEXSAN
XERJUZ	NC	1	?	0	SHELXTL PLUS
KARQUP	NC	3	?	?	SHELXTL
TOSSAV	NA	2	?	100	CRYSTAN
BIPNAP	NA	2	$x = 0.00$	0	SHELXTL
METBIW	NA	2	$x = 0.00$	100	SHELXL-93
QAFTEX	NC	3	$x = 0.00$	100	SHELXTL-96
QAF TIB	NC	3	$x = 0.00$	100	SHELXTL-96
XUQMAX	NA	1	$x = 0.38(4)$	100	SHELXL-97
HOVQAK	NC	0	$x = 0.50(3)$	100	SHELXL-93
UGARID	NC	0	$x = 0.46(12)$	100	SHELXL-97
DIYGUN	NC	3	$x = -0.14(5)$	0	SHELXL-93
GOBHEK	NA	2	$x = -0.04(5)$	0	SHELXL-93
MIRLEE	NC	1	$x = 0.08(7)$	0	SHELXL-93
GUPZOG	NA	2	$x = 0.11(7)$	0	SHELXL-97
YEQDAZ	NA	2	$x = 0.059(11)$	0	SHELXL-97
NALCIM	NC	0	$x = 0.04(12)$ $x = 0.91(12)$ for inverted structure	~15	SHELXTL
NIGGIT	NC	1	$R^+ = 3.42\%/R^- = 3.51\%$	100	CRYSTAN

?, means no value is available for this datum.

In column 2, headed S; NC, non-centrosymmetric chiral; NA, non-centrosymmetric achiral.

In column 3, headed P, the number of origin-free directions is given.

In column 5, Friedel coverage is given in percent.

measured, then the Friedel coverage is 0%. However, if for each value of  $h k l$ , both the reflection  $h k l$  and its Friedel opposite  $-h-k-l$  (or one symmetry-equivalent to it) have been measured then the Friedel coverage is 100%.

- The computer software used for the least-squares refinement.

### 3. Data analysis

We shall start by some general comments on the contents of Table 1 and follow this up by detailed analyses of all classes of results.

Referring to the symmetry-related information of the “wrong” structure in columns 2 and 3, ‘S’ and ‘P’ of Table 1, we note that there is about an equal chance that the “wrong” structure has been described as chiral or achiral, in comparison to the true crystal structure which is centrosymmetric and hence achiral. There are conditions limiting the ways in which achiral or chiral molecules can form achiral or chiral crystal structures [6]. Thus, it is very troubling to us that in no case did the report of the crystal structure in *Inorganica Chimica Acta* carry with it any information relating to the enantiopurity either of the bulk or the individual crystal used in the diffraction experiment [8]. We had high expectations of finding reports of physico-chemical measurements such as DSC, specific rotation of the optical activity, CD spectra and enantioselective chromatography. It is also the case that in general the “wrong” crystal structure has origin-free directions. As discussed more fully below, a crystal structure described with origin-free directions has more freedom to adapt to certain aspects of the diffraction pattern and it thus comes as no surprise that there is a preponderance of these in the “wrong” crystal structures.

None of the reports of the “wrong” crystal structures had an easily-accessible datum to quantify the Friedel coverage, although it was possible in all but one case to extract this value after some labour. Fifty-two percent of the “wrong” structures had a Friedel coverage of 0%. One cannot stress enough that it is good practice in structure analysis to measure at least one asymmetric region of reciprocal space and in particular for a structure presented as being non-centrosymmetric that the Friedel coverage be 100% if resonant scattering is significant. We will see the consequences of this lack of data completeness in the detailed analysis below.

Turning now to a more detailed analysis of Table 1, we note that for the set of 9 “wrong” structures (NIGKAP, TEWPUG, LAGQEP, MUJZAS, QARPUU, ABOSUF, XERJUZ, KARQUP, TOSSAV) representing 39% of the total, there is no report of any attempt to model the absolute structure of the crystal. Once again this is an important parameter for non-centrosymmetric structures showing significant resonant scattering and must be evaluated and reported in any such structure analysis [9,10].

The set of four structures (BIPNAP, METBIW, QAF-TEX, QAFTIB) has the characteristic that each is

reported with a Flack parameter of exactly zero without an associated standard uncertainty. Consequently the structure analysis used a fixed value of zero of the Flack parameter which was not subject to variation by least-squares refinement. As all of these structures were analysed using the SHELXL refinement program [11], the most likely explanation is that a TWIN command, without a BASF command, was given in the .ins instruction stream. This causes SHELXL to use a fixed value of  $x = 0.0001$  and to output a value of  $x = 0.00$  to the CIF at the end of the analysis. It is unsatisfactory to proceed in this way as the Flack parameter must be refined along with the other parameters [9,10]. So for the first 13 structures (56%) in Table 1, no attempt was made to determine the absolute structure. This is totally unsatisfactory.

For the next set of three structures (XUQMAX, HOV-QAK, UGARID) the determination and reporting is complete. Friedel coverage is 100%. The Flack parameter has been refined in each case and takes a value in the neighbourhood of 0.5 with small values of the standard uncertainties. This is what one might expect for a centrosymmetric structure treated as non-centrosymmetric with data of a Friedel coverage of 100%. The observed intensities within each Friedel pair are almost identical for a centrosymmetric structure, being exactly so if there are no systematic or statistical variations. The corresponding model intensities for any non-centrosymmetric structure are identical when  $x = 0.5$ . If observed intensities within Friedel pairs are nearly equal, a non-centrosymmetric least-squares refinement may achieve near-equality within Friedel pairs by simply moving close to a value of 0.5 for the Flack parameter. The three refinements in this set bear out this analysis. The full-matrix least-squares refinement of a centrosymmetric structure treated as non-centrosymmetric will lead to values of the Flack parameter close to 0.5 if the Friedel coverage is 100%. Conversely, a structure modelled as being non-centrosymmetric leading to a refined value of the Flack parameter close to 0.5 using data with a Friedel coverage of 100% may in fact be centrosymmetric. It should be noted however that  $x = 0.5$  corresponds to the real physical situation of a crystal which is a 50:50 twin by inversion of a truly non-centrosymmetric structure. Analysis of the atomic coordinates of the refined model permits the detection of additional symmetry operations allowing a twin to be distinguished from a centrosymmetric crystal structure.

The set of five structures (DIYGUN, GOBHEK, MIR-LEE, GUPZOG, YEQDAZ) is characterized by having origin-free directions, refined values of the Flack parameter near to zero with small standard uncertainties, Friedel coverage of 0% and refinement carried out with a version of SHELXL. At first sight, the values of the Flack parameter for this set of structures seem to indicate that one is dealing with nice single-domain crystals of truly non-centrosymmetric structures. Yet Clemente [1] is definite that these structures are centrosymmetric. We hypothesize that

if these structures had been refined against data with a Friedel coverage of 100%, the values of the Flack parameter would have been close to 0.5 as with the previous set of three structures. However, to understand how such confusing results could be obtained one needs some more background information. There is an effect discovered by Ueki et al. [12] and quantified by McDonald and Cruickshank [13] now known as the polar-dispersion error. Due to this effect one may observe appreciable apparent displacements in atomic coordinates. The effect manifests itself when there is significant resonant scattering, origin-free directions, poor Friedel coverage and inverted models. Nowadays the polar-dispersion error manifests itself in full-matrix least-squares refinement by strong correlation between the Flack parameter and the atomic coordinates along the origin-free directions. To achieve full-matrix refinement of the Flack parameter in SHELXL one must include the TWIN/BASF commands in the .ins instruction stream [14]. However, this is not the default option and none of the users of SHELXL in Table 1 stated that they had used the TWIN/BASF commands. One is thus forced to suppose that with all five structures in this set the default *hole-in-one* option was operative. The latter is not a simultaneous full-matrix refinement of all parameters and works in the following way. In a *hole-in-one* SHELXL run, several cycles of least-squares refinement are undertaken with a FIXED value of zero for the Flack parameter varying all other structural parameters simultaneously. Then the structural parameters are fixed at their refined values and the Flack parameter alone is allowed to vary for one least-squares cycle only. The final values of the atomic coordinates correspond to a value of zero for the Flack parameter and subsequent runs of SHELXL necessarily start with the Flack parameter at zero. We can now understand what happens in the refinements of this set of five structures. During the refinement of the structural parameters with the Flack parameter fixed at zero, the atomic coordinates move around to minimize the weighted sum of squares. Since the Friedel coverage is zero, the atomic coordinates along the origin-free directions move to positions biased by the polar-dispersion-error effect which compensate the non-centrosymmetric part of the resonant-scattering contribution not found in the observed centrosymmetric reflection intensities. Only one member of each Friedel pair is present so the difference between this observed and its calculated intensity is diminished whereas the virtual difference for the Friedel opposite is increased. In the subsequent single refinement cycle of fixed atomic coordinates and variable Flack parameter, again the Friedel coverage of zero is crucial implying there is no information in the data forcing the model to take equal intensity values for Friedel opposites. Consequently the Flack parameter sticks close to its initial value of zero as clearly seen for the five structures in this set. We may also safely hypothesize that no attempt was made under the same conditions to refine using an inverted crystal structure as model. A

careful study of our analysis makes it clear that a Flack parameter near to zero for both the published crystal structure and the inverted one would be obtained. A value of the Flack parameter close to zero does not mean that the *hole-in-one* algorithm is not producing adverse effects.

NALCIM is in a class by itself and it would consequently be dangerous to draw too many conclusions. The unusual characteristics of this structure determination are that a small percentage (15%) of Friedel opposites has been measured, that there are no origin-free directions, and that the authors have nevertheless reported a “refined” value of  $x$  for the inverted structure which is close to  $1 - x$ , where  $x$  is the value of the Flack parameter for the non-inverted model. It seems the Friedel coverage is too low to pull the value of  $x$  towards 0.5. One cannot tell whether the authors refined the inverted structure in obtaining the value of  $x = 0.91(12)$ .

The final set contains only one structure NIGGIT. It uses a technique in vogue before the introduction of the Flack parameter. The structure has been refined to  $R = 3.42\%$ . As the model is non-centrosymmetric, the atomic coordinates move around to soak up small systematic and statistical non-centrosymmetric perturbations in the essentially centrosymmetric data. Using inverted coordinates (i.e., the inverted non-centrosymmetric model) without further refinement,  $R = 3.51\%$  is found. As the refinement has not been allowed to converge, this  $R$  factor is higher than the fully refined model.

#### 4. Concluding remarks

In the structure analysis of a crystal presented as being non-centrosymmetric there is a real need to report and evaluate the following quantities:

- The Friedel coverage which should be close to 100%.
- The value of the Flack 1983 parameter [2] and its standard uncertainty determined by full-matrix least-squares refinement. If the structure refinement has been undertaken using one of the versions of SHELXL [11], full-matrix refinement is achieved by using the TWIN/BASF command and the report must include a clear statement that this has been done [14].

If the above conditions are fulfilled, a centrosymmetric structure refined as non-centrosymmetric will show a value of the Flack parameter close to 0.5. Moreover it is simple to detect some problems of data measurement and manipulation, and implementation of least-squares refinement of the Flack parameter, by carrying out a refinement on the inverted crystal structure under identical conditions to those used for the crystal structure. The sum of the Flack parameters of the two refinements should be exactly one. Full information on absolute-structure and absolute-configuration determination can be found in [9,10].

Further storm clouds are forming on the horizon of incorrect crystal structures. As described at a recent ACA

symposium [15], several groups working from different starting points, have noticed that some non-centrosymmetric crystal structures have been published as centrosymmetric-one might even be tempted to call this an anti-Marsh approach. In our own work we had been looking for disordered crystal structures of enantiopure compounds. The main barrier in this search was the lack of published evidence that the composition of the crystal was enantiopure. Although we found few disordered enantiopure crystal structures, there appeared to be plenty of disordered racemates. In the light of the ACA symposium it may well be that some of these disordered racemates (generally centrosymmetric) are really ordered enantiopure crystal structures (non-centrosymmetric). The implications for data measurement and treatment, and bulk and crystal characterisation are to be noted. It is advantageous to have a Friedel coverage of 100% even if the crystal structure is initially thought to be centrosymmetric, and to undertake a specific test to see if the diffraction pattern is centrosymmetric. The widespread availability of area detectors means that achieving a Friedel coverage of 100% will become commonplace. These detectors however represent a far greater advantage than just speed and coverage in measurement, and structure analysts would be well advised to learn to observe and interpret the gross features of the diffuse scattering to justify any disordered model [16,17]. Racemates are mixtures, so the enantiomeric composition of the crystals may very well be different from that of the bulk liquid or solution. The enantioexcess of the bulk and more particularly that of the individual crystals needs to be established [8].

In our own verification of Clemente's [1] contention that the crystal structures in Table 1 are indeed centrosymmetric, we have been led to understand the very real importance of R.L. Harlow's lively and stimulating distribution of an *ORTEP-of-the-Year* prize at the annual meetings of the American Crystallographic Association. Harlow's leitmotiv is that a visual and informed inspection of molecular graphical representations containing the atomic displacement parameters (drawn to scale) can

reveal many of the shortcomings of a structure determination. Harlow's message has at least been heard and acted on in some quarters.

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