

(*Z,2R,3R,4aR,7R,12aS*)-2,3,7,8,12,12a-Hexahydro-2,3-dimethoxy-2,3,7-trimethyl-4a*H*-[1,4]dioxino[2,3-*c*]oxecin-5(11*H*)-one: a commensurate occupationally modulated structure revealing a condition for diffraction symmetry enhancement for non-parent reflections

A. David Rae,* Anthony C. Willis, David T. J. Loong and Martin G. Banwell

Research School of Chemistry, The Australian National University, Canberra, ACT 2601, Australia

Correspondence e-mail: rae@rsc.anu.edu.au

Received 4 April 2005

Accepted 13 December 2005

(*Z,2R,3R,4aR,7R,12aS*)-2,3,7,8,12,12a-Hexahydro-2,3-dimethoxy-2,3,7-trimethyl-4a*H*-[1,4]dioxino[2,3-*c*]oxecin-5(11*H*)-one ($C_{16}H_{26}O_6$) crystallizes in the space group $P3_1$ and approximates the conditions necessary for diffraction symmetry enhancement without twinning for the $h - k \neq 3N$ reflections. The structure may be described as an occupancy modulation of a 1:1 disordered $P3_121$ parent structure with $Z = 3$ that would only contribute to the $h - k = 3N$ reflections. The crystal studied was a 0.717 (2):0.283 twin, but also had a stacking fault that on average caused the $(1 - p_j):p_j$ population ratio for the alternative orientations of ordered columns along the three non-equivalent screw axes ($j = 1, 2$ or 3) of $P3_1$ to be describable by $p_1 = 0.068$ (3), $p_2 = p_3 = 0.960$ (3). The effect of these stacking faults could be simulated using global parameters that modify an ordered prototype structure. The structure reveals that the ten-membered lactone ring incorporates a *Z*-configured double bond and that the methoxy-substituted stereogenic centers created during a *trans*-diol protection step each possess the *R*-configuration.

1. Introduction

During the course of a study directed towards the total synthesis of the fungal metabolite cladospolide B of known chirality, a ring-closing metathesis (RCM) reaction was carried out so as to generate an unsaturated and ten-membered ring lactone. The geometry about the double bond thus formed could not be established in a rigorous manner using NMR techniques so the material was subjected to single-crystal X-ray analysis.

1.1. Chemical background

Two of us have recently disclosed the full details associated with a chemoenzymatic total synthesis of the undecenolide cladospolide A (Banwell & Loong, 2004), a fungal metabolite exhibiting interesting plant-growth regulating properties. As part of a study to extend this work to the development of a synthesis of the stereoisomeric natural product cladospolide B (Austin *et al.*, 2005), which exhibits rather different phytochemical properties, we undertook a RCM reaction on an ester-linked 1, ω -diene in the expectation of generating a ten-membered and unsaturated lactone. It was anticipated that this product could be elaborated to the target natural product using established methodologies. In the event the RCM reaction produced a mixture of products including the chro-

Table 1

Experimental details.

| | |
|--|---|
| Crystal data | |
| Chemical formula | C ₁₆ H ₂₆ O ₆ |
| <i>M_r</i> | 314.38 |
| Cell setting, space group | Trigonal, <i>P</i> 3 ₁ |
| <i>a</i> , <i>b</i> , <i>c</i> (Å) | 18.6850 (2), 18.6850 (2), 12.2539 (1) |
| <i>V</i> (Å ³) | 3705.02 (6) |
| <i>Z</i> | 9 |
| <i>D_x</i> (Mg m ⁻³) | 1.268 |
| Radiation type | Mo <i>K</i> α |
| No. of reflections for cell parameters | 84 318 |
| θ range (°) | 2.5–27.5 |
| μ (mm ⁻¹) | 0.10 |
| Temperature (K) | 200 |
| Crystal form, colour | Prism, colourless |
| Crystal size (mm) | 0.47 × 0.32 × 0.28 |
| Data collection | |
| Diffractionmeter | Enraf–Nonius Kappa CCD |
| Data collection method | φ and ω scans with CCD |
| Absorption correction | Integration |
| <i>T_{min}</i> | 0.963 |
| <i>T_{max}</i> | 0.985 |
| No. of measured, independent and observed reflections | 98 252, 5629, 5022 |
| Criterion for observed reflections | <i>I</i> > 3.00 σ (<i>I</i>) |
| <i>R_{int}</i> | 0.055 |
| θ_{\max} (°) | 27.5 |
| Range of <i>h</i> , <i>k</i> , <i>l</i> | –24 ⇒ <i>h</i> ⇒ 24 –24 ⇒ <i>k</i> ⇒ 24 –15 ⇒ <i>l</i> ⇒ 15 |
| Refinement | |
| Refinement on | <i>F</i> |
| $R[F^2 > 3\sigma(F^2)]$, $wR[F^2 > 3\sigma(F^2)]$, <i>S</i> | 0.038, 0.048, 1.29 |
| No. of reflections | 5022 |
| No. of parameters | 707 |
| H-atom treatment | Constrained to parent site |
| Weighting scheme | Based on measured s.u.'s, $w = 1/[\sigma^2(F_o^2) + 0.0009F_o^2]$ |
| $(\Delta/\sigma)_{\max}$ | 0.1 |
| $\Delta\rho_{\max}$, $\Delta\rho_{\min}$ (e Å ⁻³) | 0.26, –0.23 |
| Absolute structure | The enantiomer has been assigned by reference to an unchanging chiral centre in the synthetic procedure |

Computer programs used: COLLECT (Nonius, 1999), HKL SCALEPACK, DENZO and SCALEPAK (Otwinowski & Minor, 1997), SIR97 (Altomare *et al.*, 1999), RAELS2000 (Rae, 2000), ORTEPII (Johnson, 1976), TEXSAN (Molecular Structure Corporation, 1992–1997), MAXUS (Mackay *et al.*, 2000).

matographically separable *E* and *Z* isomers of the desired unsaturated lactone. In the absence of definitive NMR data, the major and crystalline *Z* isomer was subjected to X-ray analysis in order to unequivocally establish configuration about the newly formed C=C double bond. The outcomes of this analysis are the subject of the discussions presented herein and serve to complement the rather limited number of other X-ray crystallographic studies on unsaturated ten-membered ring lactones formed through RCM processes (Fürstner *et al.*, 2002).

2. Experimental

2.1. Synthesis and characterization

The title compound was subject to the usual range of spectroscopic analyses including NMR studies, details of

which are presented elsewhere (Austin *et al.*, 2005). None of these allowed for the unequivocal assignment of double-bond geometry.

2.2. Data collection

The fact that the molecule was known to be chiral and asymmetric implied that the near perfect $\bar{3}1m$ symmetry of the diffraction pattern had to arise from some form of twin-disorder since volume requirements implied there were nine molecules per cell rather than 6 or 12. Systematic absences implied that *P*3₁ or *P*3₂ was the appropriate space group. Consequently, data sets were collected for three different crystals. The crystal chosen for refinement was the one that had the best *R_{merge}* value for $\bar{3}$, but the worst for $\bar{3}1m$ diffraction symmetry. The *R_{merge}* value for $\bar{3}$ was 0.055 compared with 0.114 for $\bar{3}1m$ diffraction symmetry. The reflections merged using $\bar{3}$ were separated into two groups. The subsequent *R_{merge}* values for $\bar{3}1m$ diffraction symmetry were 0.099 for $h - k = 3N$ and 0.121 for $h - k \neq 3N$. Intensities for $h - k \neq 3N$ reflections were on average 40% of those for $h - k = 3N$ reflections.

2.3. Structure solution and refinement

The structure could be solved by direct methods (SIR97; Altomare *et al.*, 1999) using the raw data and assuming the space group *P*3₁ and no twinning. The known chirality of the bulk material (Austin *et al.*, 2005) made the correct space group *P*3₁ and not *P*3₂. However, an ordered structure would not refine to an *R*(*F*) below 0.10. After choosing the origin along *c*, inspection of the structure suggested a twin-disorder model was probable using the 180° rotation (–*y*, –*x*, –*z*) about a tertiary crystal axis of this *P*3₁ structure as the twin-disorder operation (see Appendix A). The constrained least-squares refinement program RAELS2000 (Rae, 2000) was subsequently used for refinement. See Table 1 for experimental data.¹

The final refinement modelled the observed integrated intensity relative to the background at Bragg reflection positions as

$$I(\mathbf{h}) = K(\mathbf{h})^2 \{ (1 - q)[(1 - p)F(\mathbf{h}) + pF(2\mathbf{h})]^2 + q[(1 - p)F(2\mathbf{h}) + pF(\mathbf{h})]^2 \}$$

and is justified using structure-factor algebra given in Appendix A. *F*(**h**) is the structure factor for a perfectly ordered structure, **h** is *hkl*, **2h** is \overline{hkl} , *q* is a ‘twinning parameter’ and *p* is a ‘disorder parameter’. The scale *K*(**h**) has two values, *K*₁ for $h - k = 3N$ and *K*₂ for $h - k \neq 3N$. *K*₂/*K*₁ refined to 0.912 (2), *p* to 0.011 (1) and *q* to 0.283 (2). The twinning reduces the differences between twin-related reflection intensities by a factor of $1 - 2q = 0.434$ (4) compared with an untwinned crystal. The interpretation in Appendix A is in terms of population ratios for alternative orientations for

¹ Supplementary data for this paper are available from the IUCr electronic archives (Reference: CK5012). Services for accessing these data are described at the back of the journal.

ordered columns of molecules. This use of structure-factor algebra allows an ordered prototype crystal to effectively describe a twin-disorder crystal in which population distributions may vary between different regions of the crystal, as presumably do the average origin and orientation of the individual columns. Packing considerations imply that within a single column there is no disorder of molecules over 180° rotation-related positions. This approach avoids the necessity to refine minor components in the actual structure with all the associated problems of closely overlapping atoms and was inspired by the solution to a similar problem (Rae *et al.*, 2004).

The structure contains three non-equivalent columns of 3_1 symmetry in the unit cell along $1/3, 2/3, z$; $1, 1, z$; and $2/3, 1/3, z$ related by the pseudo-symmetry operation $5/3 - y, 4/3 - x, 1 - z$, and can be described as an occupancy ordering of a 1:1 disordered parent structure in the space group $P3_121$ with one third the cell volume and $Z = 3$. The origin was chosen so that the disordering operation is $-y, -x, -z$. Ordering allows each column to take up one of two orientations related by a 180° rotation about an axis perpendicular to c . The ordered prototype structure contains the pseudo-twofold screw axis $5/3 - y, 4/3 - x, 1 - z$ relating the three molecules in the asymmetric unit of $P3_1$. The atoms O17, O117 and O217 lie approximately on this screw axis. There are two columns per unit cell in one orientation, while the other column is in the alternative orientation. This creates diffraction symmetry enhancement without twinning for the $h - k \neq 3N$ reflections should the pseudo-twofold screw-axis operation relating the three molecules in the asymmetric unit hold exactly. The systematic selection between alternative orientations of columns of the structure is not always true in the actual structure (see *Appendix A*).

Various constraints were used in the refinement to reduce the number of variables and allow the H atoms to be refined. Pseudo-screw-axis-related O—Me and C—Me atom groups were constrained to have identical geometries of exact local

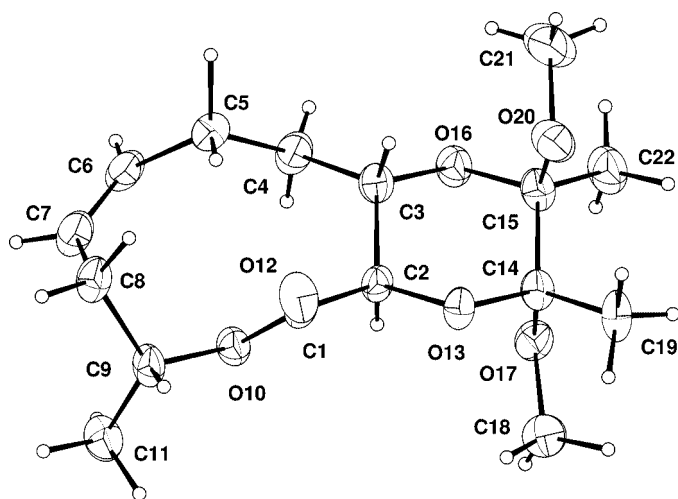


Figure 1
The atom labelling of molecule 1. Atoms in molecule 2 (or 3) include an extra integer (1 or 2) after the element (C or O or H).

Table 2
Refinement statistics.

| Class | Number | $R(F)$ | $R(F^2)$ | wR | Gof |
|-------|--------|--------|----------|-------|-------|
| 1 | 1702 | 0.035 | 0.059 | 0.047 | 1.346 |
| 2 | 3320 | 0.040 | 0.073 | 0.048 | 1.264 |
| 1–2 | 5022 | 0.038 | 0.065 | 0.048 | 1.292 |
| 3 | 607 | 0.210 | 0.386 | 0.248 | 1.072 |
| 1–3 | 5629 | 0.043 | 0.066 | 0.050 | 1.281 |

Class 1: Reflections with $I > 3\sigma(I)$ and $h - k = 3N$. Class 2: Reflections with $I > 3\sigma(I)$ and $h - k \neq 3N$. Class 3: Reflections with $I < 3\sigma(I)$. An uncorrelated 3% uncertainty in $|F|$ was included with the counting statistic uncertainty for evaluating weights $w = 1/[\sigma(F)^2 + (0.03F)^2]$. Refinement was on F .

$3m$ symmetry using constraints on refinable local coordinates defined relative to refinable local orthonormal axial systems (Rae, 1975*a,b*). Non-pseudo-equivalent O—C and C—C distances were allowed to be independent. However, only two sets of local coordinates were used for the methyl H atoms, one for all methyls attached to an O atom, the other for all methyls attached to a C atom. All non-H atoms had independent anisotropic atom displacement parameters and the H atoms were constrained to have the same parameters as the atom to which they were attached. Three sets of methyl H atoms (those attached to O20, O120 and O220) were allowed an extra libration about the relevant C—O bond that was constrained to be the same for all three sets. These constraints allowed an essentially anisotropic refinement of all atoms and used 707 variables for a reflection set of 5022 independent reflections with $I > 3\sigma(I)$ obtained after merging assuming $\bar{3}$ diffraction symmetry. It was seen that hydrogen positions were refinable and reliable geometry was obtained with reasonable standard uncertainties and with no need to apply additional restraints to differences in pseudo-equivalent bond lengths and angles. Final refinement statistics are given in Table 2.

2.4. Discussion of the structure

The structure reveals that the ten-membered ring incorporates a *Z*-configured double bond and that the methoxy-substituted stereogenic centers created during a *trans*-diol protection step each possess the same configuration. Additional features of interest include the chair-like conformation of the 1,4-dioxane ring and the axial orientations of the two attached methoxy groups, the latter no doubt arising through the operation of anomeric effects. The near orthogonal relationship between the mean plane of the ten-membered ring and the associated lactone carbonyl unit is striking and may account for the facility with which this moiety can be reduced in a subsequent step of the reaction sequence leading to cladosploide B. The absolute configuration of the title compound follows from an X-ray analysis of a chlorinated precursor as well as the sequence of reactions employed in elaborating this material (Austin *et al.*, 2005; Banwell *et al.*, 2004).

It should be noted that atom labels have not strictly followed ideas suggested by the systematic names of the compounds. Fig. 1 shows the labelling for the first of three

molecules in the asymmetric unit. The labels for the corresponding atom in the second and third molecules are obtained by including the numbers 1 or 2 after the symbol for the element, *e.g.* C1, C101, C201.

The methyl C11 (at 0.6940, 0.7007, 0.7925) and C18 (at 0.6455, 0.9896, 0.5388) atoms are associated with the column about the screw axis at $1/3, 2/3, z$ and lie approximately on what were 3_1 screw axes of the parent structure (*i.e.* at $2/3, 2/3, z$ and $2/3, 1, z$; see Fig. 2). They are related by the pseudo-symmetry operation $x, 1+x-y, 4/3-z$, which was a twofold rotation in the parent structure. Thus, the disorder operation for the relevant column interchanges C11 and C18. Atoms on these pseudo- 3_1 screw axes are the only major connections between the non-equivalent columns. The distortion that causes the $h-k \neq 3N$ reflections to lose the exact $\bar{3}m$ diffraction symmetry of the idealized model (see Appendix A) is apparently sufficient to lock in the ordered $Z=9$ structure as a dominant repeating unit during crystal growth.

A $Z=3$ structure in $P3_1$ can be created by switching the orientation of the column passing through the origin to have the same orientation as the other two columns of the $Z=9$ structure. Consequently, C11 atoms would lie along one of the two remaining 3_1 axes per cell and the C18 atoms along the other. We presume this is not a favoured event since in an

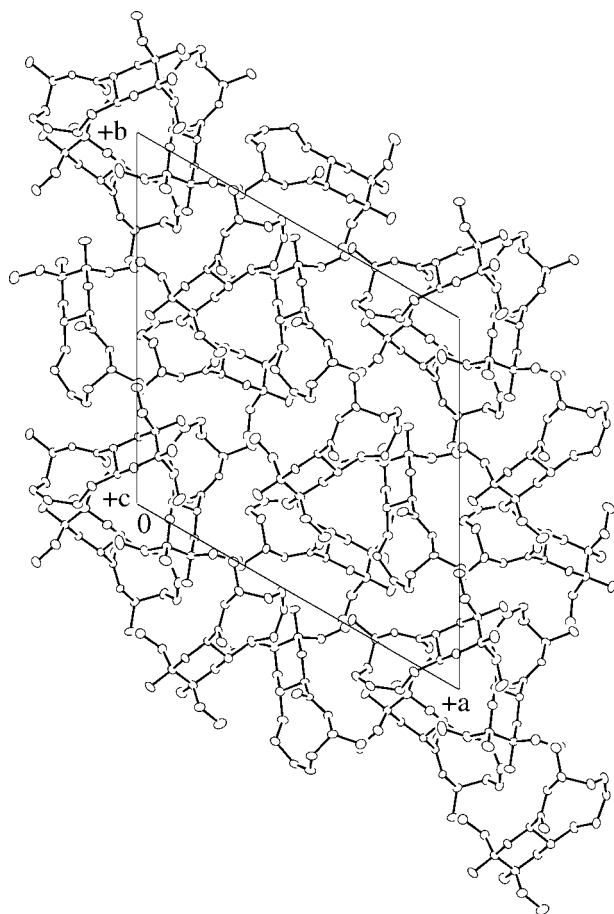


Figure 2
Cell contents viewed down *c*.

ordered, $Z=9$ structure there are two non-equivalent sets of 3_1 -related columns of methyl groups per unit cell, one set contains equivalents of C11, C118 and C211, the other contains equivalents of C18, C111 and C218. Each of the three non-equivalent 3_1 screw axes in the $Z=9$ structure is surrounded by six columns of methyl groups, three of each type. If the orientation of either of the two other columns per unit cell is switched, the nature of the adjacent columns of methyl groups is also switched, *e.g.* columns now contain equivalents of either C18, C118 and C211 or C11, C111 and C218. This allows both a localized disorder (switch of an individual column) and a twinning mechanism, *i.e.* adjacent layers perpendicular to \mathbf{a}^* are switched from the orientation sequence $ABAABA\dots$ to the orientation sequence $ABBABB\dots$

The finer details of the structure modulation have to be qualified by the fact that we are looking at a twin-disorder structure and the quality of structure parameters is necessarily compromised. However, the methods used in our refinement have allowed the data to be fitted using an ordered prototype model and refinable structure-factor algebra to combine pseudo-equivalent reflections of this structure to simulate the diffraction intensities. As this method is novel, only very limited constraints and restraints were used (see earlier) in order to see if the predicted errors in bond lengths and angles were reasonable by comparing the values of pseudo-equivalent geometric features. The largest range for any bond length was 0.025 \AA for the C1–O10 bonds, which was *ca* six times the standard uncertainty of an individual bond. This implies the means of such geometric features are chemically meaningful. The torsion angles C15–C14–O17–C18, $172.3(2)$, C115–C114–O117–C118, $179.2(3)$ and C215–C214–O217–C218, $181.1(3)^\circ$ allow an easy adjustment for the stacking of columns and appear to be significantly different. However, the pseudo-equivalents of C18 (and C11) make a limited contribution to reflections with $h-k \neq 3N$. The range of torsion angles can be compared with that for C14–C15–O20–C21, $-175.2(3)^\circ$, C114–C115–O120–C121, $-176.4(3)^\circ$ and C114–C115–O120–C121, $-178.9(3)^\circ$. The pseudo-screw axes of a column of methyl groups are each significantly displaced from the positions $1/3, 1/3, z$ and $2/3, 2/3, z$ by *ca* 0.3 \AA towards $1, 1, z$. A contributor to this result is the rotation of the columns at $1/3, 2/3, z$ and $2/3, 1/3, z$ in opposite directions so that these columns are no longer related by a translation. These observations imply that in an ordered $Z=3$ crystal structure, the distance from the origin to an adjacent column of C11 atoms would prefer to be longer than the distance from the origin to an adjacent column of C18 atoms. This supports our earlier conjecture that the avoidance of columns of only C11 or only C18 is a building principal for crystal growth.

APPENDIX A

Effect on intensities of stacking faults

The $P3_1$ structure can be described as a partial ordering of a 1:1 disordered parent structure in the space group $P3_121$ with

one third the cell volume and $Z = 3$. The twofold axis creates the 1:1 disorder by relating alternative orientations of columns. An ideally ordered structure contains two parallel columns of $P3_1$ symmetry and a third column in the alternative orientation. The origin can be chosen so that a pseudo-twofold screw axis $5/3 - y, 4/3 - x, 1 - z$ relates the three molecules in the asymmetric unit of $P3_1$ locating column 2 at $1/3, 2/3, z$, column 1 at $1, 1, 1 - z$ and column 3 at $2/3, 1/3, z$. The translation $1/3(\mathbf{a} - \mathbf{b})$ relates columns 2 and 3.

If there is no induced displacement accompanying this occupational modulation, we can evaluate a simple functional form for the resulting structure factors $F(\mathbf{h})$ that reveals diffraction symmetry enhancement for the $h - k \neq 3N$ reflections, irrespective of the actual ordering. This idealized model is now elaborated.

We say that $F_1(\mathbf{h})$ is the structure factor for an ordered column passing through the origin and we choose the origin along \mathbf{c} so that a twofold rotation through the origin creates the alternative orientation for that column. Consequently,

$$F(\mathbf{h}) = [(1 - p_1) + \omega(1 - p_2) + \omega^*(1 - p_3)]F_1(\mathbf{h}) + [p_1 + \omega p_2 + \omega^* p_3]F_1(\mathbf{2h}),$$

where $\omega = \exp[2\pi i(h - k)/3]$, $\omega^* = \exp[-2\pi i(h - k)/3]$ and $(1 - p_j):p_j$ gives the population ratio for the alternative orientations of column j ($j = 1, 2$ or 3). The perfectly ordered structure corresponding to our listed coordinates has $p_1, p_2, p_3 = 0, 1, 1$. Values for p_1, p_2, p_3 of $1, 0, 1$ and $1, 1, 0$ correspond to different origin choices. Structures related by a twofold rotation through the origin are obtained by swapping the values of $(1 - p_j)$ and p_j .

When $h - k \neq 3N$

$$F(\mathbf{h}) = [p_1 + \omega p_2 + \omega^* p_3][F_1(\mathbf{2h}) - F_1(\mathbf{h})]$$

and

$$F(\mathbf{2h}) = [p_1 + \omega^* p_2 + \omega p_3][F_1(\mathbf{h}) - F_1(\mathbf{2h})]$$

so that

$$I(\mathbf{h}) = I(\mathbf{2h}) = P_1^2 |F_1(\mathbf{h}) - F_1(\mathbf{2h})|^2,$$

where $P_1^2 = p_1^2 + p_2^2 + p_3^2 - p_1 p_2 - p_2 p_3 - p_3 p_1$. For a perfectly ordered idealized structure $I(\mathbf{h}) = I(\mathbf{2h}) = |F_1(\mathbf{h}) - F_1(\mathbf{2h})|^2$ and $F(\mathbf{h}) = -F(\mathbf{2h})$. We see that diffraction-symmetry enhancement without the need for twinning is possible for these reflections should the pseudo-symmetry operations hold exactly. Disorder scales the observed intensity.

When $h - k = 3N$

$$F(\mathbf{h}) = 3/2[F_1(\mathbf{h}) + F_1(\mathbf{2h})] + P_2[F_1(\mathbf{2h}) - F_1(\mathbf{h})]$$

and

$$F(\mathbf{2h}) = 3/2[F_1(\mathbf{h}) + F_1(\mathbf{2h})] - P_2[F_1(\mathbf{2h}) - F_1(\mathbf{h})]$$

so that

$$[I(\mathbf{h}) + I(\mathbf{2h})]/2 = 9/4|F_1(\mathbf{h}) + F_1(\mathbf{2h})|^2 + P_2^2|F_1(\mathbf{2h}) - F_1(\mathbf{h})|^2$$

and

$$[I(\mathbf{h}) - I(\mathbf{2h})]/2 = 6P_2^2[|F_1(\mathbf{2h})|^2 - |F_1(\mathbf{h})|^2],$$

where $P_2 = p_1 + p_2 + p_3 - 3/2$.

If we preserve the value of $p_1 + p_2 + p_3$ as 2 then $P_2 = 1/2$ and $P_2^2|F_1(\mathbf{2h}) - F_1(\mathbf{h})|^2$ is ca 10% of $[I(\mathbf{h}) + I(\mathbf{2h})]/2$ on average. Any disorder will probably make P_2^2 tend to zero.

We see that there are inherently three well determined global parameters, namely P_1 and P_2 associated with the column packing as well as a twinning parameter q . Note that there are only two degrees of freedom and setting $p_2 = p_3$ is of no consequence. The first parameter controls the scale of the $h - k \neq 3N$ reflections, the second and third, the scale of $[I(\mathbf{h}) + I(\mathbf{2h})]/2$ and $[I(\mathbf{h}) - I(\mathbf{2h})]/2$ for the $h - k = 3N$ reflections.

Any adjustment to fit $[I(\mathbf{h}) - I(\mathbf{2h})]/2$ for the $h - k \neq 3N$ reflections defines displacements away from positions imposed by the idealized pseudo-symmetry operation $5/3 - y, 4/3 - x, 1 - z$ relating the columns and has a scale that correlates with P_1, P_2 and q .

Our first model assumed that $P_2 = 1/2$ and refined a twin ratio $(1 - q):q$ and a separate scale for $h - k \neq 3N$ reflections to modify the structure factors of a perfectly ordered prototype structure. The twinning to multiply $[I(\mathbf{h}) - I(\mathbf{2h})]/2$ by $1 - 2q = 0.434$ (4) rather than 1.0 implies a twofold screw axis perpendicular to \mathbf{c} must be involved in creating a truly twin-disorder structure. The relative scaling of $h - k \neq 3N$ reflection amplitudes by $P_1 = K_2/K_1 = 0.896$ (3) would imply the value of $P_1^2 = 0.803$ (6) when averaged over twin-related mosaic blocks.

Our second model said $I(\mathbf{h}) = (1 - q)[(1 - p)F(\mathbf{h}) + pF(\mathbf{2h})]^2 + q[(1 - p)F(\mathbf{2h}) + pF(\mathbf{h})]^2$, where $F(\mathbf{h})$ is the structure factor for a perfectly ordered structure. The disorder parameter p and the twin parameter q were refined using *RAELS2000* (Rae, 2000). This twin-disorder model used a single scale for all reflections and a twofold axis through the origin simulated a disorder of $(1 - p):p$ in column 1 and of $p:(1 - p)$ in columns 2 and 3. This implies $p_1 = p$ and $p_2 = p_3 = 1 - p$ implying that $P_1^2 = (1 - 2p)^2$ and $P_2 = (1 - 2p)/2$. This refinement improved the data fit for $h - k = 3N$, but made it worse for $h - k \neq 3N$ and suggested that two scales should still be used.

A final model including two scale constants refined successfully and implies that when averaged over mosaic blocks of crystal $P_1^2 = [(1 - 2p)K_2/K_1]^2$ and $P_2 = (1 - 2p)/2$. The final refinement gave values of $p = 0.011$ (1), $q = 0.283$ (2), $K_2/K_1 = 0.912$ (2), implying $P_1 = 0.892$ (3) and $P_2 = 0.489$ (1). A solution obtained assuming $p_2 = p_3$ makes $p_1 = 0.068$ (3) and $p_2 = p_3 = 0.960$ (3).

References

- Altomare, A., Burla, M. C., Camalli, M., Cascarano, G. L., Giacovazzo, C., Guagliardi, A., Moliterni, A. G. G., Polidori, G. & Spagna, R. (1999). *J. Appl. Cryst.* **32**, 115–119.
 Austin, K. A., Banwell, M. G., Loong, D. T. J., Rae, A. D. & Willis, A. C. (2005). *Org. Biomol. Chem.* **3**, 1081–1088.
 Banwell, M. G., Edwards, A. J. & Loong, D. T. J. (2004). *ARKIVOC*, (x), 53–67.
 Banwell, M. G. & Loong, D. T. J. (2004). *Org. Biomol. Chem.* **2**, 2050–2060.

- Fürstner, A., Radkowski, K., Wirtz, C., Goddard, R., Lehmann, C. W. & Mynott, R. (2002). *J. Am. Chem. Soc.* **124**, 7061–7069.
- Johnson, C. K. (1976). *ORTEP-II*. Report ORNL-5138. Oak Ridge National Laboratory, Tennessee, USA.
- Mackay, S., Gilmore, C. J., Edwards, C., Stewart, N. & Shankland, K. (2000). *MAXUS*. Nonius, The Netherlands, MacScience, Japan, University of Glasgow, Scotland.
- Molecular Structure Corporation (1992–1997). *TEXSAN*, Version 1.8. MSC, 3200 Research Forest Drive, The Woodlands, TX 77381, USA.
- Nonius (1999). *Collect.* Nonius BV, Delft, The Netherlands.
- Otwinowski, Z. & Minor, W. (1997). *Methods Enzymol.* **276**, 307–326.
- Rae, A. D., Linden, A., Majchrzak, A., Mloston, G. & Heimgartner, H. (2004). *Acta Cryst.* **B60**, 416–423.
- Rae, A. D. (1975*a*). *Acta Cryst.* **A31**, 560–570.
- Rae, A. D. (1975*b*). *Acta Cryst.* **A31**, 570–574.
- Rae, A. D. (2000). *RAELS2000*. Australian National University, Canberra, Australia.