Proc. Indian Acad. Sci. (Chem. Sci.), Vol. 97, No. 2, September 1986, pp. 209–211.

Solution of difficult crystal structures: New, simple, economic and time saving approaches†

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MS received 2 July 1986

Abstract. MULTAN is the most widely used package for structure determination. However, there are situations where even after utilizing all possible built-in routes the solution is not reached and these become "difficult structures". If such a structure (a) has one or more heavy atoms, (b) is "chicken-wire" with predominant aromatic character, (c) has weak diffraction data, the new approaches discussed will lead to a unique structure solution by introducing simple, economic and time saving ideas into the MULTAN package.

Keywords. Difficult crystal structures; new approaches; MULTAN package.

During the last two decades, advances in structure determination via "Direct Methods" have made extensive progress in terms of automation and several standard packages are currently in use. One such widely used package is MULTAN (Germain *et al* 1971) which normally leads to a unique structure solution in a single automatic run. Several versions of MULTAN are now in use and we shall restrict ourselves to MULTAN 78 (Main *et al* 1978), the version currently available in our laboratory. MULTAN 78 comprises mainly of four routines, NORMAL, MULTAN, FFT and PEAKSEARCH. In case a routine automatic run of MULTAN 78 fails, there are several alternate suggested built-in routes which involve increasing the total number of E values, modifying temperature factors, increasing the number of reflections in the starting set, feeding-in known chemical information, using a fragment for recycling of phases, giving correctly known orientation or partial position information etc. When all these approaches fail, we have a "difficult structure" and at this stage, normally the user tends to give up this structure determination.

The philosophy underlying the new methods suggested below for such difficult situations involves a careful study of the characteristics of the structure, the constituents of the molecule, systematic features in data sets and above all a non-mechanical use of MULTAN. In addition, these methods aim at a reduction of the computer time and memory budget, and the total man hours. The net effect, however, is an unambiguous structure solution. The following are the various steps involved in solving a structure.

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†NCL Communication No. 4099

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(a) *Structures with heavy atom(s)*

Step 1: Convert the data set either to the triclinic system or use the representative Patterson space group (monochilic : $P2/m$, orthorhombic: $Pmmm$ etc.) for analysis.
Step 2: Input a pseudo-fragment with one of the heavy atoms at (0, 0, 0) and four hydrogen atoms at arbitrary positions, since the FFT package needs a minimum of five atoms input to NORMAL.
Step 3: Compute FFT with F_{observed} values (effectively $|F|$ synthesis). The limits in the PEAKSEARCH program have to extend to half the unit cell so as to get all possible interactions.
Step 4: From these interactions the heavy atom positions can easily be deduced and subsequent runs of FFT in the original space group will give the structure.

This entire operation takes 3 min (3000 reflections) on an ICL1904S machine. The procedure at the outset is not very different from a Patterson synthesis. However, the ease with which the structure can be obtained without any bias to incorrect assumptions about space group symmetry, incorrect information on the constituents of the structure or slips in interpreting the Patterson function, makes this a unique one. A somewhat similar approach is already in use (Buerskens *et al* 1984) but the methodology explained above also takes care of reduction in computer time and memory. A routine MULTAN run takes approximately 30 min for a structure with about 50 atoms.

(b) *Structure with predominant aromatic character (rings)*

Step 1: A routine MULTAN run to start with to get a "chicken-wire" solution.
Case (i): Only one aromatic ring.
Step 2: Generate equivalent data to get a triclinic system.
Step 3: Fix one of the atoms at (0, 0, 0) and shift the other ring atoms without changing the orientation as obtained from step 1, "chicken-wire" run.
Step 4: Compute the Fourier map using FFT in $P1$, locate the symmetry and generate the corresponding molecule or the molecular fragment. Use this information to get the rest of the atoms in the structure using the FFT run in the original space group.
Case (ii): Two or more aromatic rings. Only three different orientations of any two fused aromatic rings are possible. All three are subjected to the procedure under case (i) and one of these will generate the entire structure. The choice of only two fused rings is adequate to arrive at the correct structure even in cases with many rings.
Case (iii): A large number of aromatic rings with one ring containing a heavy atom.

The above procedures described under (a) and (b) may not work due to a large number of parallel vectors. After case (i) step 2, the heavy atom is placed at (0, 0, 0) and the ring formed around the heavy atom also has only three possibilities. The geometry around the heavy atom is adjusted to the standard values and the procedure under case (i) is repeated to get the entire structure.

Each of these operations take only 2 to 3 min of computer time after the initial routine run (about 30 min).

Table 1. Examples* of structures solved by these methods.

	Code**				
	RUTH	IITB	MOGHE	IYDY	ALBA
Molecular formula	$C_{42}H_{39}ClO_2.P_2S_2RU$	$C_{19}H_{25}NO_2$	$C_{18}H_{23}N_2O_3Cl$	$C_{26}H_{16}SO_2$	$C_{39}H_{32}O_8$
Method	a	b(i)	b(ii)	b(iii)	c
Space Group	$P\bar{1}$	*Pcab*	$P\bar{1}$	$P\bar{1}$	$P2_12_12_1$
a(Å)	10·042(1)	7·781(1)	6·037(1)	7·500(2)	28·337(5)
b	11·216(1)	9·959(1)	10·208(3)	9·164(1)	15·961(5)
c	17·772(2)	43·031(4)	15·499(3)	14·330(2)	8·188(4)
α (deg)	99·80(1)	90	103·98(2)	108·06(1)	90
β	93·26(1)	90	82·68(2)	83·71(1)	90
γ	90·86(1)	90	108·56(2)	100·72(1)	90
Z	2	8	2	2	4
R	0·078	0·057	0·062	0·063	0·156

** RUTH, communicated to *Polyhedron;*
IITB, communicated to *Acta Crystallogr. (C)*;
MOGHE, communicated to *Acta Crystallogr. (C)*;
IYDY, *Dyes and Pigments* **7** 81 (1986);
ALBA, *Tetrahedron Lett.* **24** 3013 (1983).
* Several structures have been solved in our laboratory by these methods and this table gives only one example per method.

(c) *Weak diffraction data*

These situations occur while dealing with structures of natural products since in these cases getting a good crystal is often a severe limiting step. There will be very few reflections for a decent 'Direct Method' run. The procedure described below is for non-centric space groups.

Step 1: About 30–40 highest E values (including origin specifiers and enantiomorphs) are given random equal phases (for example $\phi = 20°$; $\phi = 30°$; $\phi = 40°$).
Step 2: A routine run of MULTAN for all these three cases is done and from the map a repetitive fragment (4 or 5 atoms) is extracted.
Step 3: A Karle recycling is run on this fragment to get additional atoms and then a routine FFT yields the entire structure.

Table 1 gives examples for each of these methods. In conclusion, it is felt that these modified procedures would be of immense value to a practising crystallographer with even a small computer and a limited budget.

References

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