

gruppe am Benzolring die freie Drehbarkeit der Carbonamidgruppe weitgehend aufhebt. Käme es zur Ausbildung einer intramolekularen Wasserstoffbrückenbindung zwischen N(1) und O(1), dann wäre die freie Drehbarkeit ebenfalls aufgehoben, und es wäre auch kein Chiralitätszentrum mehr vorhanden, da die Carbonsäureamidgruppe in die Benzolringebene zu liegen käme. NMR-Untersuchungen in unterschiedlich polaren Lösungsmitteln dürften zeigen, ob diese Konformation ohne intramolekulare Wasserstoffbrückenbindung nur für die kristalline Phase charakteristisch ist.

Die Bindungsabstände entsprechen im allgemeinen den in der Literatur (*International Tables for X-ray Crystallography*, 1962) angegebenen Werten. C(17)–N(2) ist gegenüber C(17)–N(3) um 0,08 Å aufgeweitet. Der Grund dafür scheint zu sein, dass die Sulfonylgruppe elektronenziehend wirkt und den Doppelbindungscharakter der N–C-Bindung weitgehend aufhebt.

Von den Kohlenstoffatomen des Cyclohexanringes hat nur C(18) einen Temperaturfaktor in der gewohnten Größenordnung, alle anderen haben doppelt so grosse Temperaturfaktoren, was in Verbindung mit der Differenzfouriersynthese auf eine grosse Beweglichkeit dieser Atome hinweist. Für C(24) ist dann ein noch grösserer Temperaturfaktor zu erwarten, was auch beobachtet wird. Ähnlich grosse Temperaturfaktoren wurden auch in Cyclododecan gemessen (Dunitz & Shearer, 1960), wo keinerlei Baeyer- und Pitzerspannung und auch keine bemerkenswerte transannulare Wechselwirkung festzustellen ist. Unter diesen Voraus-

setzungen neigen cycloaliphatische Gruppen anscheinend dazu, nur wenig starre Gebilde darzustellen. Der Fehler von Bindungslängen zwischen Atomen mit aussergewöhnlich grossen Temperaturfaktoren ist sicherlich grösser, als man nach der Standardabweichung erwarten sollte.

Sehr viele Vertreter der Benzamido-alkyl-benzol-sulfonyl-harnstoffe wurden auf ihre pharmakologische Wirkung als Antidiabetika untersucht (Weber *et al.*, 1969). Dabei zeigte es sich, welche Gruppen die pharmakologische Wirkung erhöhen können. Es dürfte interessant sein, die damals gemachten Erfahrungen unter der Annahme neu zu durchdenken, dass die im Kristallverband der untersuchten Verbindung gefundene Konformation mit der in Lösung identisch oder ihr zumindest sehr ähnlich ist.

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PSST: a Combination of Patterson Superposition and Σ_2 Techniques for Phase Determination

BY ROBERT K. WISMER AND ROBERT A. JACOBSON

Ames Laboratory-USAEC and Department of Chemistry, Iowa State University, Ames, Iowa 50010, U.S.A.

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A method of phase determination which utilizes both the Σ_2 relation and Patterson superposition technique has been developed. Reflections input into the initial Σ_2 relation are used to compute a map upon which the shifted Patterson is superimposed. The Fourier transform of the resultant map, with negative regions set equal to zero, yields reliable phases for the larger $|E|$ values. These are then extended and refined by usual direct-method techniques. Application of this method to both a centric and an acentric structure is presented. Further refinements and extensions of the method are also discussed.

Introduction

At present there are two methods commonly used for solving structures of moderate complexity. Direct methods, such as those using the Σ_2 relation (Karle & Karle, 1966), are primarily reciprocal-space methods,

while methods based on the deconvolution of the Patterson function (for a detailed bibliography see Buerger, 1959) are primarily real-space methods.

There is a certain parallelism between these two methods and both have their advantages and disadvantages. Both involve some initial choices which

can greatly influence the success of the method. The Σ_2 relation can be readily programmed and many automatic or semi-automatic procedures have been developed based on this relation. However, it is usually difficult to make use of known structural information in this approach. Furthermore, if no reasonable structure is produced, the investigator has little recourse but to modify his choice of origin-determining reflections or to closely examine those phases selected at the early and most critical part of this phase determination procedure. With Patterson methods, on the other hand, there are usually a greater number of options initially available corresponding to differing modes of selection of peaks for superposition. Also, known structural information can be more readily introduced, since a real-space representation is being employed. For complex structures, however, large numbers of superpositions are generally required and severe degradation of the structural image can result due to the accumulation of errors in the atom position selections.

The advent of the fast Fourier transform technique and its application to crystallography (Hubbard, Quicksall & Jacobson, 1972) allows rapid real space – reciprocal space conversions. Thus, it is appropriate to consider whether a hybrid direct method–Patterson method approach having greater power than either method alone can be developed. It is just such a hybrid that we wish to describe here.

Theoretical basis of the method

In direct methods employing the Σ_2 relation, one starts with E 's of large magnitude so that phases will be determined with reasonably high probabilities. Owing to the fact that the initial contributors are few in number, erroneous phase indications may still result which then propagate in the phase determination procedure. Consider the map produced by a Fourier transform using as non-zero coefficients only those reflections input into the Σ_2 relation (henceforth this map will be referred to as the Σ_2 -map). For the phase determination procedure to be successful, it is necessary that the square of this Σ_2 -map better resemble the true electron-density function than does the Σ_2 -map itself. If so, the phases of the transformed coefficients with larger magnitudes should be good approximations to the phases of the corresponding large $|E|$'s.

Since the initial set of E 's is very small in number, possibly only the three origin-determining reflections, it is the characteristics of the Σ_2 -map that should be closely examined. First, if large $|E|$'s are used, there is a high probability that atoms will lie on, or at least near, some of the maxima occurring on this map. Second, there will be a large number of extraneous maxima on the square of the Σ_2 -map – a number far exceeding the number of atoms in the cell. The first is an asset and the second a liability for successful phase determination. These extraneous peaks come from either maxima or minima on the Σ_2 -map. It is the

presence of these extra peaks that greatly inhibits the production of additional phase information.

One would like to modify the square of the Σ_2 -map so that it better resembles the electron-density function. An obvious modification is to eliminate all negative regions (or possibly regions lower than a certain lower bound) by setting these regions equal to zero before squaring. Indeed, this technique has been applied by Barrett & Zwick (1971) to some extent in the extension and refinement of crystallographic protein phases.

In the initial applications of the Σ_2 relation, there are so few phased E 's that even with the modification described above, there are large positive regions in many areas of the map which do not correspond to atomic locations. However, the Patterson function contains images of the structure with each atom in turn at the origin. Therefore, if an atomic position can be selected on the Σ_2 -map, a superposition of the appropriately scaled Patterson map on this position should produce a map with considerably fewer extraneous peaks and with much better resemblance to the electron-density function. If such a map is then squared to emphasize the higher peaks and transformed, better and more extensive phase information will result. Once a sufficiently large set of phased E 's has been obtained the remaining $|E|$'s can be efficiently phased by normal application of phase extension and refinement techniques of the Σ_2 type.

Application of the method

(a) Centric case

The compound β -picoline-*N*-oxide fumaric acid adduct (Gorres, 1964) was chosen as a centrosymmetric test case. We felt this would be a good test case as the structure had previously been solved only with difficulty by use of a roving model-vector verification technique after usual superposition and symbolic-addition procedures had not proved successful.

This adduct crystallizes in the space group $P2_1/c$ with $a = 3.888$, $b = 14.194$, $c = 14.666$ Å and $\beta = 98.85^\circ$. There are two adducts of formula $C_{16}H_{18}N_2O_{12}$ per unit cell, *i.e.* the adduct has a center of symmetry. Values of $|E|$ were computed in the ordinary way and there were 270 $|E|$'s greater than 1.0. The three selected origin-determining reflections are given in Table 1. These three along with the symmetry-related reflections were used in a Σ_2 -map calculation ($32 \times 32 \times 32$ grid points). Some typical sections of this map are shown in Fig. 1.

Table 1. Origin-determining reflections for the centric test case (β -picoline-*N*-oxide fumaric acid adduct)

<i>h</i>	<i>k</i>	<i>l</i>	$ E $	Sign
1	0	2	4.17	+
3	1	3	2.53	–
1	14	–5	2.14	+

The positions of the five highest peaks on this map were noted and in each case checked by examining the Patterson for the presence of vectors between symmetry-related atoms. In each case, such vectors were found and indeed these peaks fell approximately (within 0.5 Å) at the positions of four carbon atoms and a nitrogen atom in the structure.

All the negative regions in the Σ_2 -map were then set equal to zero and five independent superpositions were carried out by placing the origin of the Patterson at each of the five peak positions and the symmetry-related points. A sharpened Patterson function was

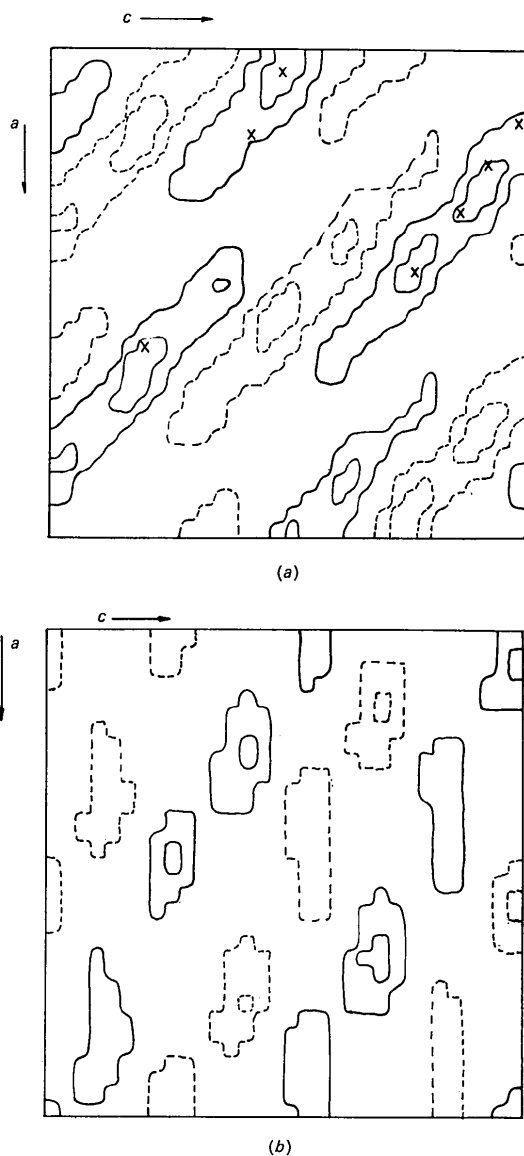


Fig. 1. Typical sections of a Σ_2 -map for β -picoline-*N*-oxide fumaric acid adduct. (a) Composite constructed by adding layers 3,4,5; — contoured at 40 and 80; ---- contoured at -40 and -80. Atom positions indicated by X. (b) Layer 9; — contoured at 15 and 25; ---- contoured at -15 and -25. No atoms in or near this section.

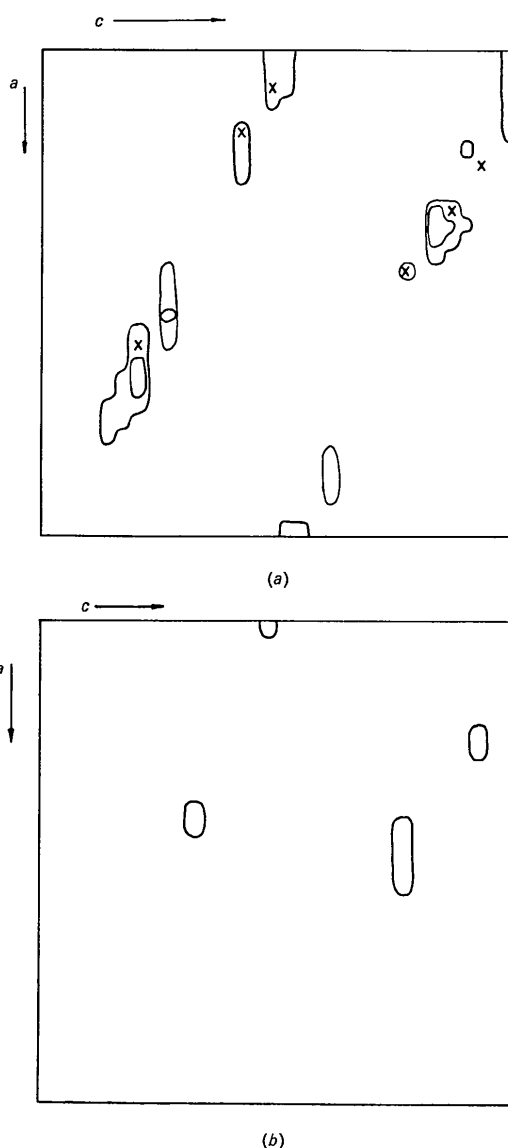


Fig. 2. Results of Patterson map superimposed on Σ_2 -map of Fig. 1 at the four nitrogen equivalent positions. (a) Composite of layers 3,4,5; — contoured at 9 and 18. Atom positions indicated by X. (b) Layer 9; — contoured at 5. No atoms in or near this section.

used and the minimum procedure employed (Hubbard & Jacobson, 1968). The scale of the Patterson was adjusted so that the value of the highest off-origin peak on the Patterson map was approximately equal to the value of the highest off-origin peak on the Σ_2 map. Fig. 2 shows some typical results using the peak corresponding to the nitrogen atom position as the superposition point.

Each of the five maps was then squared and the resulting transform coefficients (G_{hkl}) calculated using a fast Fourier algorithm (Hubbard *et al.*, 1972). Only the 50 reflections with the largest values of the product $|E^*G|$ and with $|E| > 1.50$ were kept. Some typical

results are shown in Table 2. The signs determined for each hkl were then averaged. (In some cases more than 80% of the 50 largest $|E|$'s were signed correctly in the individual sets.) These signed reflections were then used to compute a new Σ_2 -type map, and negative regions were set equal to zero. The transform of the square of this map was used to obtain signs (92% of which were correct) for input at the 90% confidence level into a phase-extending program (Main, Woolfson & Germain, 1971). The resulting complete set of 270 phases was used to compute a map from which the positions of all the non-hydrogen atoms in the structure were readily determined. There were no significant spurious peaks on this map.†

(b) *Acentric case*

The compound chosen as a test for the acentric case was D-glucono-(1,5)-lactone (Hackert & Jacobson, 1971), which crystallizes in the space group $P2_12_12_1$ with axial lengths $a=7.838$, $b=12.322$, $c=7.544$ Å. Of the 1259 unique observed reflections, 435 have $|E|$ greater than 1.0. Three origin-determining reflections were selected ($|E|=2.39$, 2.51, 2.04), two of which were non-zonal reflections. To make the test a reasonably severe one, no enantiomorph-selecting reflection

was included; the enantiomorph was chosen as part of the superposition procedure.

The Σ_2 -map produced from these and their symmetry-related reflections showed more than 25 large peaks, all of which had relative heights between 120 and 185. The relative height of the other peaks on this map was less than 90. However, only eight of these peaks generated appropriate Harker vectors in the Patterson. Of these eight, four were clearly in one enantiomorph, since they remained when the superposition point was a member of the set.

Using these four peaks and proceeding in a manner similar to the centric case above, the average phases of the 30 largest $|E^*G|$'s with $|E| > 1.40$ were obtained. Some typical results for this acentric structure are given in Table 3. The transform of the square of the expanded Σ_2 -map yielded initial phases for the 50 largest $|E^*G|$'s with $|E| > 1.40$. These phased $|E|$'s were then input into a phase extending program at the 90% confidence level. In the resulting set of 410 phased E 's, 390 were within 40° of the published phases and their transform readily revealed all the non-hydrogen atomic positions. As in the centric case, there were no significant spurious peaks on this final map.

Extensions of the method

Since we wished to give the method a reasonably severe test, only three origin-determining reflections were used for the initial Σ_2 -map calculation in each case. Other

† This method has now been used to solve the structure of diisopropyl-(2,3,4,5-tetraphenylcyclopenta-2,4-diene) phosphate, $P2_1/c$, 160 non-hydrogen atoms per cell (Krishnamachari & Jacobson, to be published).

Table 2. *Representative results† obtained for a centric test case (β -picoline-N-oxide fumaric acid adduct)*

h	k	l	$ E $	1	Calculated signs				Known sign
					2	3	4	5	
-2	10	4	3.25	-	+	+	+	+	+
-1	11	7	3.13	-	+	+		+	+
0	11	9	3.00	-		+			+
0	12	4	2.94				+		-
-1	10	12	2.80	-	-	-	-	-	-
1	10	8	2.73	+	-	-		-	-
-2	4	12	2.63				+		+
1	11	7	2.55	+	-			-	-

* The absence of a calculated sign indicates that the value of $|E^*G|$ for that reflection was smaller than the limit used.

Table 3. *Representative results† obtained for an acentric test case [D-glucono-(1,5)-lactone]*

h	k	l	$ E $	1	2	3	4	Known phase
								phase
0	3	6	3.48	270	270	270	270	270
0	4	3	2.67	0	180	180	180	180
0	7	9	2.58		90	90	90	90
0	11	2	2.36	89				90
2	2	6	2.22		277		256	296
1	7	5	2.19			276	284	293
0	4	0	1.95	179				0
3	-3	-7	1.77	179			177	197
1	-3	-2	1.59	282	83	100	90	81
0	2	3	1.58	179	0		0	180
3	4	2	1.64		267		278	316
4	-9	-1	2.04	230	243	220	256	262
2	4	6	1.56	84	88		91	114

† The absence of a calculated phase indicates that the value of $|E^*G|$ for that reflection was smaller than the limit used.

reflections, phased by either Σ_2 or Σ_1 relations (and perhaps with appropriate weights), can also be included to produce peaks of greater reliability. In the centric case, those Σ_1 reflections which were determined with greater than 90% probability were included in the calculation of the Σ_2 map. Their addition improved the phase agreement to a small extent. The frequency check procedure (Gorres & Jacobson, 1964) can be applied to the Σ_2 -map.

It also is possible to include an additional strong reflection with the origin-determining reflections, thus producing two Σ_2 maps in the centric case, for example. The resulting two sets of averaged phases could then be handled in a similar way as in those direct-methods programs that produce multiple solutions.

Lower bounds other than zero can be used for modification of the resultant superposition map. Indeed, some calculations for the centric example have shown that use of a lower bound of 10% of the maximum peak height results in somewhat improved agreement.

From Tables 2 and 3, it is obvious that a straight average is a poor procedure compared with a more judicious method of averaging. Preliminary computations indicate that in the centric case a requirement of a net of two like signs produces a significant improvement in the percentage of correct signs selected.

The phases are also somewhat sensitive to grid point resolution of the maps. In the centric structure, calculations were run using a grid of $0.12 \times 0.45 \times 0.45$ Å resolution. Results improve if a resolution of approximately 0.25 Å is used in all three directions.

Squaring the resultant superposition map appears to give the best phases compared with other powers which could be employed. All exponents from 0.2 to 6.6 in steps of 0.2 were examined for a typical run, with 2.0 appearing the most satisfactory.

Conclusion

We feel that these results demonstrate the effectiveness of an approach which utilizes advantages of both direct and Patterson methods and in doing so avoids many of their limitations.

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The Crystal Structure of Magnesium Chlorophosphate, $\text{Mg}_2(\text{PO}_4)\text{Cl}$

BY J. R. REA* AND E. KOSTINER†

Baker Laboratory of Chemistry, Cornell University, Ithaca, New York 14850, U.S.A.

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Magnesium chlorophosphate, $\text{Mg}_2(\text{PO}_4)\text{Cl}$, crystallizes in the space group $Pna2_1$, with unit-cell dimensions $a = 10.940$ (1), $b = 7.9305$ (6), and $c = 4.8008$ (4) Å ($Z = 4$). A three-dimensional structural analysis using automatic-diffractometer data has been completed and refined by full-matrix least-squares procedures to a residual $R = 0.025$ ($R_w = 0.044$). The compound is isostructural with the previously reported $\text{Mn}_2(\text{PO}_4)\text{Cl}$.

Introduction

In a continuing investigation of the crystal chemistry of halophosphates of composition $\text{M}_2(\text{PO}_4)\text{X}$ (M is a

divalent metal, X is a halogen) (Rea & Kostiner, 1972*a*, *b*), we have grown single crystals of magnesium chlorophosphate $\text{Mg}_2(\text{PO}_4)\text{Cl}$ and determined its crystal structure.

The preparation of $\text{Mg}_2(\text{PO}_4)\text{Cl}$ has been reported (Klement & Haselbeck, 1965) but, aside from the reported similarity of its X-ray powder-diffraction pattern to that of $\text{Mn}_2(\text{PO}_4)\text{Cl}$, no structural work has been done.

* Present address: Mary Baldwin College, Staunton, Virginia, U.S.A.

† Author to whom correspondence should be addressed at: Department of Chemistry and Institute of Materials Science, University of Connecticut, Storrs, Connecticut 06268, U.S.A.