Table 1. $\mathscr{R}_{b,n-m,\alpha}$ *and the differences* $1000(\mathscr{R}^{\text{approx}}-\mathscr{R})$

b	$n-m$	$\alpha=0{\cdot}50$		$\alpha=0{\cdot}25$		$\alpha=0{\cdot}10$		$\alpha=0{\cdot}025$		$\alpha=0{\cdot}01$	
2	480	1·001	0	1·003	−1	1·005	−2	1·008	−3	1·010	−3
3	480	1·002	0	1·004	0	1·007	−1	1·010	−1	1·012	−2
5	480	1·005	−1*	1·007	0	1·010	−1	1·013	0	1·016	−1
10	480	1·010	0	1·013	0	1·017	0	1·021	0	1·024	0
2	240	1·003	−1	1·006	−2	1·010	−3	1·015	−4	1·019	−6
3	240	1·005	−1	1·009	−1	1·013	−1	1·020	−3	1·024	−3
5	240	1·009	0	1·014	0	1·019	0	1·027	−1	1·032	−1
10	240	1·019	0	1·026	0	1·033	0	1·043	0	1·049	−1
15	240	1·030	−1*	1·038	0	1·046	0	1·057	0	1·064	0
2	120	1·006	−2	1·012	−3	1·019	−5	1·031	−10	1·039	−12
3	120	1·010	−1	1·017	−1	1·026	−2	1·040	−5	1·048	−5
5	120	1·018	0	1·028	−1	1·039	−1	1·054	−1	1·064	−2
10	120	1·038	0	1·052	0	1·067	−1	1·086	0	1·098	−1
20	120	1·078	0	1·097	0	1·117	0	1·142	0	1·157	0
2	40	1·017	−4	1·035	−9	1·059	−17	1·097	−31	1·122	−38
3	40	1·030	−3	1·052	−4	1·080	−7	1·122	−13	1·150	−16
5	40	1·054	−2	1·083	−2	1·118	−3	1·167	−5	1·200	−7
10	40	1·112	0	1·154	−1	1·200	−1	1·264	−2	1·304	−2
20	40	1·221	0	1·280	0	1·343	−1	1·426	0	1·478	−1

* These differences do not indicate growing trends in variation, but are caused by smaller differences being rounded off in different directions.

Most tables of the F distribution do not cover adequately the region where $n-m$ is large, and interpolation is necessary. To avoid this we can make use of an approximation for F given by Lindley & Miller (1953). To calculate $\mathscr{R}$ at the α probability level we require x_α, the α-probability point of the normal distribution (one tail):

α	0·50	0·25	0·10	0·05	0·01	0·005	0·001
x_α	0·0000	0·6745	1·2816	1·6449	2·3263	2·5758	3·0902 .

Defining

$$\lambda=(x_\alpha^2-3)/6$$

and

$$h=2/(b-1)^{-1}+(n-m-1)^{-1}),$$

$$F=\exp\{2[x_\alpha(h+\lambda)^{1/2}/h-((b-1)^{-1}-(n-m-1)^{-1})\,(\lambda+5/6)]\}\,.$$

Then

$$\mathscr{R}^{\text{approx}}_{b,n-m,\alpha}=\left[\frac{b}{n-m}\,.\,F+1\right]^{1/2}.$$

This is obviously very easy to calculate in any constrained refinement program, and if we do use it we should know its range of validity.

For a typical example $n-m\sim900$ but b can range from 1 to $\sim m$. The approximation is invalid for $b=1$, but from $b=2$ onwards it improves as b increases. We therefore investigate for increasing b until the error in $\mathscr{R}^{\text{approx}}$ is negligible. The comparison table (Table 1) gives values for $\mathscr{R}_{b,n-m,\alpha}$ taken from Hamilton (1964) and also the differences in the last digit between these values and the approximate values. In this table the maximum value of 480 for $n-m$ is the maximum in Hamilton's tables. Clearly the approximation is very good for $n-m>240$ for $b>5$. Even for smaller values of $n-m$ and/or b the approximation is surprisingly good. However the table should speak for itself and provide a useful guide.

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Application of Patterson methods to the solution of molecular crystal structures containing a known rigid group.

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The rotational and translational parameters of a known molecular rigid group in an unknown crystal structure have been determined using reciprocal-space methods based on the Patterson function. Various refinements of the rotation function have been introduced in order to increase the speed and sensitivity of this method.

A number of methods have been proposed for interpreting the Patterson function of crystals containing a molecular fragment of known internal geometry, *e.g.* Hoppe (1957) and Nordman & Nakatsu (1963). The rotation function

(Rossmann & Blow, 1962) has been widely used in the investigation of protein structures and its successful applications include horse haemoglobin (Rossmann & Blow, 1962), insulin (Dodson, Harding, Hodgkin & Rossmann, 1966), seal myoglobin (Tollin, 1969) and aldolase (Eagles, Johnson, Joynson, McMurray & Gutfreund, 1969). In the work described here this function, together with the Q-function of Tollin (1966), has been applied to the solution of a 32-atom molecular structure, *i*-cholesteryl chloroacetate (Fig. 1, X=Cl).

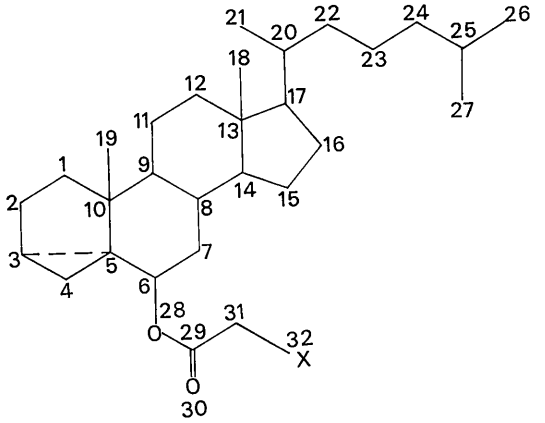

Fig. 1. The 6β-acetyl-*i*-cholesterol skeleton.

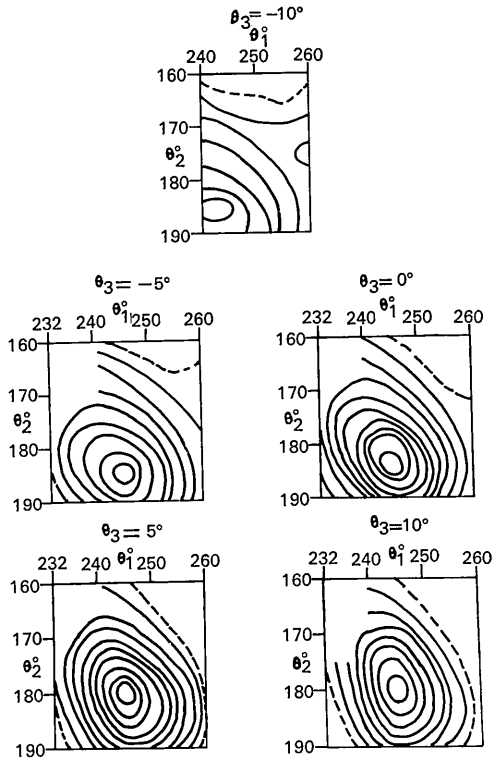

Fig. 2. The rotation function for *i*-cholesteryl chloroacetate in terms of the Cartesian angles θ_1, θ_2, θ_3, in the vicinity of the correct peak.

The rotation function determines the orientation of a known structural fragment in an unknown structure by measuring the degree of overlap between the arbitrarily rotated fragment self-Patterson and the observed Patterson function within a volume U centred on the origin. When the vector sets of the fragment in both Patterson functions coincide, it is hoped that a rotation function maximum will be produced. In our case, the known fragment is the 21-atom [C(1)–C(20), O(28)] rigid group of *i*-cholesteryl bromoacetate (Fig. 1, X=Br), the geometry of which was obtained from the heavy-atom solution of the full orthorhombic structure (Harrison, Hodgkin, Maslen & Motherwell, 1970). The unknown structure, *i*-cholesteryl chloroacetate, space group $P2_1$, had been solved independently with non-centrosymmetric direct methods (Harrison & Motherwell, 1970). To obtain well-resolved Patterson peaks and hence good rotation function resolution, it was found necessary to employ $|E|^2$ (Karle & Karle, 1966) rather than the normal $|F|^2$ for both known and unknown. In a previous unsuccessful solution attempt the use of $|F|^2$ as coefficients gave a maximum in approximately the desired region, but the peak was quite distorted and packing considerations excluded the corresponding rotation. Subsequent structure determination showed all three rotational parameters to be in error by 10–15°.

The expression for the rotation function in reciprocal space in terms of the $|E|^2$ may now be written as:

$$R = \sum_P |EP|^2 \left(\sum_h |E_h|^2 G_{h,h'} \right) \qquad (1)$$

where $G_{h,h'}$ is the magnitude of the Fourier transform of the volume U. The known Patterson coefficients ($E_h|^2$ were calculated using a hypothetical $P1$ unit cell of constants $a=c=9{\cdot}5$, $b=16$ Å, $\alpha=\beta=\gamma=90°$, with the long dimension of the fragment made parallel to **b**. Since the rigid group approximates a rectangular parallelepiped $\sim 4\times 7{\cdot}5\times 4$ Å, this choice of cell dimensions and fragment orientation results in clear separation of the Patterson intramolecular and intermolecular vectors. The volume U reflects the envelope of the rigid group and was therefore taken to be a rectangular parallelepiped $9\times 15\times 9$ Å. This volume, slightly smaller than that of the hypothetical cell, excludes possible contributions to the rotation function from neighbouring Patterson origins. The unknown Patterson function was approximated with the largest $350|E_P|^2$, since it was found that they adequately represented the sharpened full-data (1900 reflexion) Patterson without introducing large series-termination effects.

The program used for the calculation of R was written in Fortran for the Oxford KDF-9 computer, the inner summation in (1) being taken over 27 points. Because of the computational time involved, it is desirable to restrict the calculation of R to as small a region of rotation space as possible (Tollin, Main & Rossmann, 1966). With the high resolution available in small molecule work and a knowledge of fragment geometry, visual pre-examination of the calculated and observed Pattersons may exclude many rotations from consideration. In the present work the characteristic steroid 1·54, 2·5 and 3 Å multiple vectors were used to predetermine three most likely rotation regions. Because they were more easily visualized and directly applicable to restricted searches, Cartesian, rather than Eulerian, angles were used to describe the rotations of the rigid group about the three triclinic axes. Using a 5° grid, all three regions of R were calculated and found to contain

single peaks, indicating the strength of the multiple regular vectors. The correct peak (Fig. 2) was the sharpest of the three and, after subtraction of mean background, was 25% larger than the other two. The exact rotational parameters were determined with a 1° grid and these were then used to calculate the relative fractional coordinates of the fragment in the unknown ($P2_1$) cell.

The absolute position of the correctly orientated rigid group was found using the $Q(X_0Z_0)$ function (Tollin, 1966) with the 350 largest $|E_P|^2$ (Fig. 3). This function uses a modified sum function (Buerger, 1959) to express the correlation of the cross vectors between symmetry related molecular fragments with the observed Patterson. For a structure containing a 2_1 axis, a spurious peak will occur if there is a pair of atoms in the known group whose y coordinates differ by $\frac{1}{2}$. Seven such false peaks were expected and are marked with an 'X' in Fig. 3. The correct peak, which fixes the position of the fragment relative to the crystallographic 2_1 axis, is marked with a '+'.

The resulting atomic position were compared with those obtained from least-squares refinement and found to be in error by from 0·03 to 0·23 Å. Calculation of an $|F_{obs}|$ synthesis using the trial coordinates clearly revealed the positions of C(29), O(30), C(31), Cl(32), C(21), C(22), and C(23), virtually completing the structure solution.

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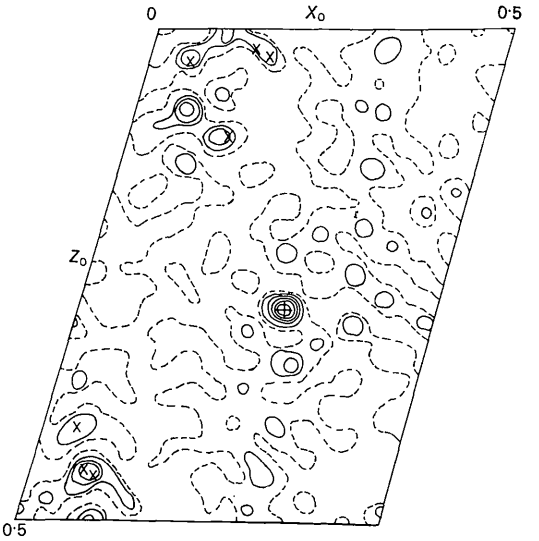

Fig. 3. $Q(X_0Z_0)$ for *i*-cholesteryl chloroacetate. × indicates the false peaks. + indicates the correct peak.

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Weak extra peak in rocking curves of X-ray reflexion for incident beams obtained by successive asymmetric reflexions.

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A numerical calculation is made on the intensity distribution of the beam obtained from the X-ray collimator system of monolithic silicon crystal, in which double 422 asymmetric Bragg-case diffractions of Cu $K\alpha_1$ take place successively. It is concluded that a weak subsidiary peak found in the rocking curve obtained with a double-crystal diffractometer of parallel setting using a collimator of the above type is caused by the relative angular shift of the range of total reflexion for each crystal component due to the refraction effect.

In a previous paper (Kohra & Kikuta, 1968), we reported a monolithic collimator system, by which a substantially parallel X-ray beam of an angular spread of 0·1 or 0·01″ can be obtained. This collimator consisted of three crystal components prepared from a single block of silicon crystal, in which double or triple 422 asymmetric Bragg-case diffractions of Cu $K\alpha_1$ radiation take place successively. As its application, we also reported the measurement of rocking curves for the 422 reflexion from silicon single crystals with various asymmetry factors, using this collimator in place of the first crystal in a double-crystal diffractometer of parallel

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