XRC83 program package for structure determination of organic molecules and drugs by single crystal X-ray diffraction

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The program package for EC computers was developed for determination of crystal and molecular structures and for stereochemical interpretation of molecular structure. This crystallographic software is optimized and user oriented. In case of drugs this system extends possibilities for studying three dimensional structure—biological activity relationships.

Была создана система программ для счётчиков ЕС серии для полного решения структур кристаллов и стереохимического объяснения молекулярных структур. Это кристаллографическое программное обеспечение (software) полностью оптимализировано с аспекта потребителя. В случае лекарств эта система расширяет возможности для изучения соотношений строение—биологическая активность.

An X-ray structure analysis has recently become the most powerful method for structure determination of organic compounds [1]. For drugs structural information alone or in combination with methods of theoretical conformational analysis can be used as a starting point for analyzing the relationships between structure and biological activity and in this way also serves as a rational base for design and development of new drugs with required properties [2—4]. This paper deals with the development of the crystallographic program package for EC computers, with which a complete X-ray structural analysis can be carried out as well as all necessary calculations for crystallochemical interpretation of molecular structure. This system of programs will make it possible for nonspecialists in crystallographic computing to solve crystal and molecular structures.

An overall organization of XRC83 program package

The XRC83 is an integrated program package which was formed by combination of modified NRC programs [5] and newly written programs. It is divided into

a greater number of programs relatively small in term of core requirement. These programs operate on a file (from here on called NRC file), in which all basic crystallographic data are stored: cell dimensions, wavelength of X-ray radiation, symmetry matrices, scattering factors and diffraction data (diffraction indices *hkl*, structure factors $|F_o|$, $\sin^2 \Theta$, $\sigma(F)$, and so on). That means that all structure invariants are calculated only once when generating this file and all necessary data are picked out from this file by individual programs. The program system is flexible, new programs can be easily added or old modified for introducing the latest methods. Only XDRF has a more complicated segmented structure.

The parts of more generally thought system are program packages developed by other authors: MULTAN80 [6]. SHELX76 [7], and DIRDIF [8] and all these packages operate on standard data file, which is generated by supporting programs. In the standard data file only basic diffraction data are stored: h, k, l, $|F_o|$, $\sigma(F)$ written as card images. The overall organization of programs is presented in Fig. 1.

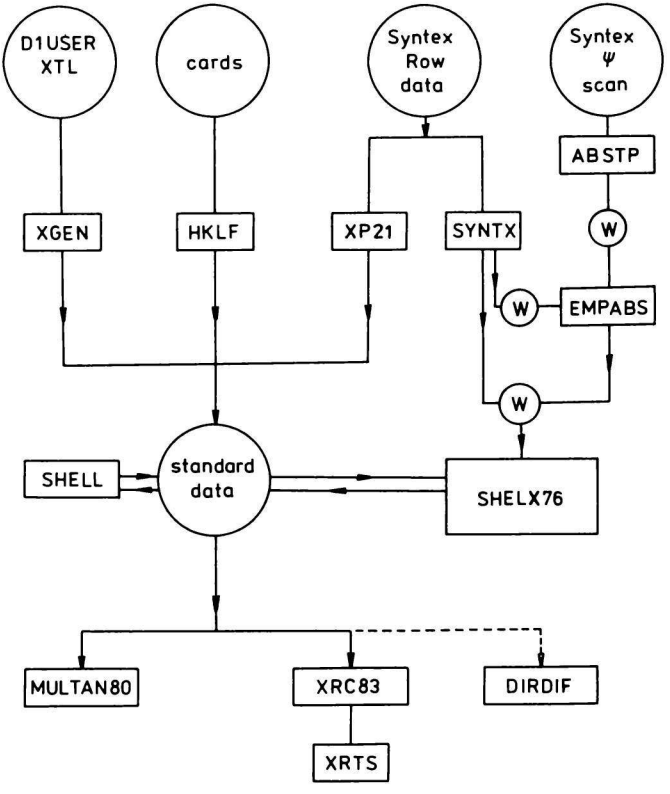

Fig. 1. Overall organization of the program system. Data files are designated by rings and programs by rectangles. For functions of programs see the text.

This configuration of the system from the independent packages has some advantages:

— MULTAN80 is one of the best program packages for direct methods;

— SHELX76 is an excellent program for routine X-ray structure analysis;

— DIRDIF is a direct method program for partially known structures;

— a Patterson map produced by XDRF can be analyzed by XRTS, that is a program for localization of molecular fragment by rotational and translational search [9].

This configuration effectively reduces an amount of programming work and it is opened for introducing the most recent program versions.

Brief description of individual programs of XRC83 program package

The list of programs and their mutual connection is in Fig. 2. The functions of individual programs are as follows:

XGEN — reads the diffraction data file from magnetic tape, which was generated by Syntex XTL programs, and generates standard data file.

HKLF — rewrites diffraction data punched in nonstandard format to standard data file.

XN02 — is modified NRC—2 program. It generates NRC file, which is then input to all XRC83 programs.

XDRF — is a program for calculation of various types of Fourier syntheses of electron density (γ', difference, $m\,F_o - n\,F_c$, α, β, and others and in case of weighted syntheses it applies weights according to *Sim* [10] or *Woolfson* [11]), and Patterson syntheses (normal, sharpened, and origin-removed). The program has routines for peak-picking, transformation of peaks to atomic parameters, and calculation of interatomic distances and angles. The program has a user friendly and optimized input.

XN10, XBLS — are the programs for refinement of positional coordinates, temperature and occupational factors by block-diagonal approximation of the least-squares method. XBLS has an optimized input and can determine an absolute configuration. XN10 is a slightly modified NRC—10 program.

XFLS — is the program for refinement of positional coordinates and temperature factors by the full-matrix least-squares method.

XN51, XN52, XN53, XN54, XN55 — are programs for direct methods. They can be used for calculating scale and overall temperature factor by Wilson statistic, calculating E values, Σ_2 relationships, application of tangent formula and Karle recycling. These programs are practically not modified NRC—5 programs.

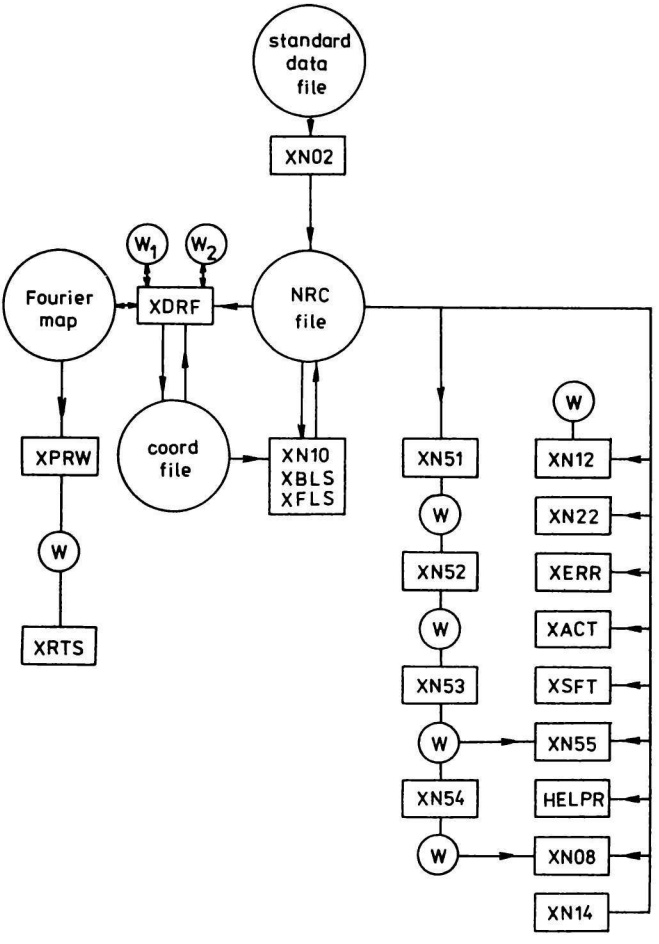

Fig. 2. A scheme of XRC83 program system. Data files are designated by rings (W — working file) and programs by rectangles. For functions of programs see the text.

XN08 — is a modified NRC—8 program for Fourier summation.

XN14 — is a modified NRC—14 program for error analysis.

XERR — is a program for weighting scheme analysis, correction for empirical extinction, and for analyzing of error distribution as a function of $|F_o|$ and $\sin^2 \Theta$. It calculates R indices.

HELPR — is a multipurpose program. It calculates coordinates of hydrogen atoms, prints point projection of molecular structure and rotates the molecule.

XN12 — is a modified NRC—12 program. It calculates interatomic distances, bond angles, and standard deviations.

XN22 — is a modified NRC—22 program. It calculates mean planes through selected atoms, atom deviations from these planes, dihedral angles, torsion angles, and standard deviations.

XACT — prints tables of coordinates, temperature factors and structure factors in a form suitable for publication in *Acta Crystallographica*.

XSFT — produces tables of structure factors in easy-to-read format.

XEDIT — is a program for modification of crystallographic files with fixed record length. It deletes, exchanges and includes records. It copies and prints files.

XPRW — reads Patterson map from a file generated by XDRF program and rewrites it to a form suitable for XRTS program.

XP21 — is a program for reduction of experimental Syntex P21 diffraction data. It generates standard data file.

SYNTX, ABSTP, EMPABS — are programs for empirical absorption correction by ψ scan [12].

SHELL — is a program for reducing the standard data file on basis of Θ angle [13].

Program instructions (in Slovak or Czech) were published separately [14].

Discussion

XRC83 is an integrated package for all basic calculations in a course of crystal structure determination and for crystallochemical and stereochemical interpretation of results.

For solution of the phase problem there are both direct and Patterson methods in the package. The direct methods are besides MULTAN80 program also in XRC83 and SHELX76. Direct methods in XRC83 are suitable for pedagogical purposes. SHELX76 includes good "black box" direct methods for centrosymmetric structures. Patterson methods are represented by rotational and translational search. The rotational function can be used for determination of molecular fragment orientation. Its position in unit cell can be found by translational function or with the help of MULTAN80 program.

The program XDRF was recently completely rewritten and this new program, XFPI85, has a routine for the high order image seeking function [15]. To the best of our knowledge this is the first general superposition program with simple input and with automatic interpretation of maps. Preliminary experiences showed that the symmetry function can be used for interpretation of Patterson function with subsequent automation of the heavy atom method.

Programs for refinement of structure by least-squares method are standard crystallographic programs. XBLS can be used for determination of an absolute configuration of chiral molecules. This is of partial interest in 3D-structure activity

relationships. Interpretation programs can carry out all necessary computing (bond lengths, angles, torsion angles, and mean planes) for evaluation of molecular structure and conformations.

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