High-Pressure Studies of Crystalline Amino Acids and Simple Peptides

Elena V. Boldyreva
REC-008 Novosibirsk State University & Institute of Solid State Chemistry and Mechanochemistry SB RAS
Kutateladze, 18, Novosibirsk, 630128, Russia
E-mail: boldyrev@nsu.ru

Received 17 November 2006/Accepted 24 November 2006

Abstract
The contribution reviews recent data on the high-pressure studies of crystalline amino acids and small peptides in relation to the effects of high pressure on biopolymers. The data on the bulk compressibility, on the anisotropy of lattice strain, on the compressibility of hydrogen bonds are discussed. Examples of pressure-induced polymorphic transitions are considered in relation to the conformational changes in biopolymers.

Keywords: amino acid, dipeptide, hydrogen bond, phase transition, compressibility, high pressure

1. Crystalline amino acids as biomimetics

Crystalline amino acids and simple peptides have been always considered as biomimetics. At the edge of X-ray structural analysis, at the beginning of the 20th century, the structures of crystalline amino acids were studied, in order to find the bond lengths, valence and torsion angles of the “primary building blocks” of proteins. By 1950s, the crystal structures of many amino acids were solved [1]. These data were used when refining the first crystal structures of proteins, since the diffraction data that could be collected for biopolymers at that time were of low resolution.

After direct high-resolution structural studies of proteins became possible, interest in crystalline amino acids decreased until very recently. A renewed interest in crystalline amino acids was related to the attempts to simulate electron charge density distribution in biopolymers using amino acids and simple peptides as model systems, in order to work out some transferable parameters and potentials [2-5]. Another research direction was related to using these systems and their packing patterns as mimetics of selected folds and interaction patterns of biopolymers. As important landmarks, one can mention the reviews [6-9], in which the typical zwitter-ions conformations, hydrogen bond patterns and packing patterns in the structures of crystalline amino acids were summarized. A careful study of the crystal structures of commonly occurring amino acids, and their racemates and complexes reveals that each hydrogen bond connecting the α-amino and the α-carboxylate groups and its symmetry equivalents generally give rise to an infinite head-to-tail sequence in which the two groups are periodically brought into close proximity (see examples in Fig. 1). Such sequences, which have been suggested to be of probable relevance to prebiotic polymerisation, appear to be an almost universal feature of amino acid aggregation in the solid state. These sequences belong to two main categories in terms of the geometrical arrangement of amino acid molecules in them. The sequences in the first category consist of straight chains of molecules related mostly by the shortest cell translation in the crystals. The sequences
of the second category form hydrogen bonded two fold helices centred around crystallographic $2_1$ screw axes. The sequences can be further sub-divided into different types on the basis of the geometrical features of the hydrogen bonds involved in them. A few sequences involving both L and D isomers have also been observed in the crystal structures of some DL-amino acids. The shortest cell translation in most crystals under consideration has a value in the neighbourhood of 5.3 Å and corresponds to the periodicity of a straight head-to-tail sequence or, less frequently, that of a helical sequence or both. The crystal structures of amino acids and their complexes can be classified in terms of the occurrence and the geometrical disposition of different types of head-to-tail sequences in them [7].

Fig. 1. Examples of head-to-tail chains of amino acid zwitter-ions in crystal structures: a) glycine, b) L-alanine, c) L-serine, d) DL-serine, chain of L-zwitter-ions, e) L-leucine
The “head-to-tail chains” are further linked via hydrogen bonds with each other. The three-dimensional crystal structures can be built as stacked layers (double centrosymmetric layers resulting in alternating hydrophobic and hydrophilic regions, or parallel layers in polar structures), three-dimensional frameworks, triple helices linked with each other, or nano-porous three-dimensional structures with hydrophobic or hydrophilic cavities of tunable size and shape that can incorporate various guest molecules (see examples in Fig. 2).

Fig. 2. Examples of crystal structures of amino acids and simple peptides: a) $\alpha$-glycine, b) $\beta$-glycine, c) $\gamma$-glycine, d) L-leucine, e) L-cystine, f) $\alpha$-glycilglycine
Crystalline amino acids can provide models, allowing one to simulate various features of biopolymers in a wide range – from those of the main backbone frameworks in fibrils and rigid robust amyloid structures to those of cavities in globular proteins. Due to the presence of the head-to-tail chains as the main structure-forming unit, the structures of crystalline amino acids resemble in many respects the structures of polyaminoacids and of the fragments of peptides, although the zwitter-ions within a chain in the crystals of amino acids are linked by dipole-dipole interactions and hydrogen bonds, but not by peptide bonds. Two-dimensional hydrogen-bonded layers in the structures of crystalline amino acids and small peptides can be compared with β-sheets in proteins and amyloids [10-14], as well as with two-dimensional crystalline layers at the interfaces [15,16]. Biomolecular assemblies (polyaminoacids, two-dimensional peptide layered structures, peptide nanoporous structures) form a link between proteins and crystalline amino acids [17]. Nano-porous structures can mimic cavities in proteins [18-20]. One can also prepare crystals, in which selected functional groups and side chains are located with respect each other in the same way, as at the recognition sites of substrate-receptor complexes, and one can use these systems, to simulate the mutual adaptation of the components of the complex responsible for the recognition process. It is important, that one can mimic not the static structures only, but also their dynamic properties – conformational transitions, changes of folds, denaturation, renaturation of biopolymers can be understood better if lattice dynamics, phase transitions, amorphization of crystalline amino acids and small peptides are studied. Variable temperature and variable pressure are important instruments in such studies.

2. Variable-pressure studies of crystalline amino acids

The variable-pressure Raman spectroscopy studies of amino acids, mainly of those with non-linear optical and piezoelectric properties, were pioneered by a group in Brazil [21,22]. In the early 2000s, systematic X-ray diffraction and spectroscopic studies of crystalline amino acids and small peptides at non-ambient conditions were started by joint efforts of Novosibirsk and Marburg Universities, using both the laboratory facilities, and the instrumentation available at Swiss-Norwegian Beamline of ESRF [23-39]. Very soon afterwards, some other groups have joined research in the same field [40-46].

High-pressure studies of crystalline amino acids and small peptides can be of interest, in order to compare: i) the bulk compressibility of different structures, ii) the compressibility of selected types of hydrogen bonds / structural syntheses, iii) the conformational flexibility of selected molecular fragments / structural syntheses, iv) the stability of selected structures with respect to phase transitions, including the effects of medium (solvent) v) the mechanisms of the phase-transitions. Many problems related to the effect of pressure on crystalline amino acids are related to similar problems considered when studying proteins at high pressures (Table 1). An advantage of crystalline amino acids as compared to biopolymers is that they can be studied in much detail at atomic resolution level; compressibility of hydrogen bonds, as well as the conformational flexibility of molecular fragments, can be measured reliably.

2.1. Bulk compressibility
Compressibility (bulk compressibility) is not only one of the basic quantitative characteristics of the response of a structure to pressure, but it also gives a new insight into dynamical properties. For example, compressibility measurements are widely applied to study protein dynamics in solutions, which contributes to biological function of protein molecules [47-55]. For crystals, compressibility can be calculated from X-ray diffraction data on the changes in cell parameters versus pressure. For the same phase, within its range of stability, compressibility was measured for α- [24,41], β- [56], and γ- [24,41] polymorphs of glycine, for L-serine [34,39,46], DL-serine [37,39], L-cysteine [45], hexagonal L-cystine [42], α-glycylglycine [44], L-alanine, DL-alanine [57], β-alanine [58] (Fig. 3). Despite different crystal structures, the values of bulk compressibility are rather close for these systems, volume change being about 5 % / GPa. L-cysteine is probably the only pronounced outlet up to now – its compressibility is noticeably higher [45]. The values can be compared with the compressibilities of proteins reported in the literature: 1 % / GPa [47-49,59-63].

Table 1. Comparison of high-pressure studies of crystalline amino acids / proteins

<table>
<thead>
<tr>
<th>Problem</th>
<th>Crystals of amino acids</th>
<th>Proteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Compressibility</td>
<td>Bulk compressibility (the structure as a whole);</td>
<td>Bulk compressibility (the structure as a whole);</td>
</tr>
<tr>
<td></td>
<td>Anisotropy of structural strain, linear compression / stretching along selected directions;</td>
<td>Compressibility of main chains, cavities, hydration contributions;</td>
</tr>
<tr>
<td></td>
<td>Compressibility of selected structural elements (molecular chains, layers, intermolecular hydrogen bonds, “empty voids”);</td>
<td>Comparison of the compressibilities of different structural fragments (helices, sheets, turns, non-structured fragments);</td>
</tr>
<tr>
<td></td>
<td>Comparison of the compressibilities of different polymorphs (different structural arrangements of the same amino acids);</td>
<td>Comparison of the compressibilities of fragments built by different sequences of amino acids.</td>
</tr>
<tr>
<td></td>
<td>Comparison of the compressibilities of crystal structures of different amino acids – effect of side chains.</td>
<td></td>
</tr>
<tr>
<td>Stability with respect to pressure</td>
<td>Stability with respect to phase transitions / amorphization;</td>
<td>Stability with respect to conformational changes / denaturation;</td>
</tr>
<tr>
<td></td>
<td>Reversible / irreversible phase transitions;</td>
<td>Reversible / irreversible changes in the secondary structure;</td>
</tr>
<tr>
<td></td>
<td>Effect of loading intensity / rate;</td>
<td>Effect of loading intensity / rate;</td>
</tr>
<tr>
<td></td>
<td>Phase transitions on compression / decompression; role of cycling;</td>
<td>Phase transitions on compression / decompression; role of cycling;</td>
</tr>
<tr>
<td></td>
<td>Effect of pressure-transmitting medium;</td>
<td>Effect of pressure-transmitting medium;</td>
</tr>
<tr>
<td></td>
<td>Thermodynamic / kinetic factors.</td>
<td>Thermodynamic / kinetic factors</td>
</tr>
</tbody>
</table>

2.2. Anisotropy of lattice strain

Much more information can be obtained, if not only the bulk compressibility is studied, but the anisotropy of structural strain is followed. Linear strain in the directions of the three principal axes of strain ellipsoids, as well as in any other selected direction in the
structure, can be calculated from the measured changes in cell parameters versus pressure, as described in [26,64,65] (Fig. 4).

![Fig. 3. Relative volume changes (%) versus pressure (GPa) in selected crystalline amino acids and in α-glycylglycine. Black – α-glygly [44], red – α-gly, green – γ-gly (full symbols [24], open symbols [41]), dark blue – L-ser [34], light blue – DL-ser [37], light violet – hexagonal L-cystine [42], pink – L-cysteine [45].](image)

![Fig. 4. Linear strain (%) in the directions of the three principal axes of strain ellipsoids versus pressure (GPa) in selected crystalline amino acids and α-glycylglycine (colors are as in Fig. 3)](image)
The analysis of the anisotropy of strain reveals the directions, in which the structure is rigid, and the directions, in which it is softer. For example, the structure of \( \gamma \)-glycine is about 2.5 times less compressible along the head-to-tail chains, than in the plane normal to these chains [24]. The structure of \( \alpha \)-glycine is also the most rigid in the direction along the head-to-tail chains [24]. The same holds for L-serine (its structure is 3 times more rigid along the head-to-tail chains, than normal to them) [34,37], and for hexagonal L-cystine (compressibility normal to the plane, in which the head-to-tail chains are located is 1.5 times higher, than within this plane) [42]. In \( \alpha \)-glycilglycine, the structure expands slightly (+0.6 % at 4.7 GPa) along the head-to-tail chains), and contracts in directions normal to these chains (at about -3.62 % and –12.6 % along the two principal directions of the strain ellipsoid), as can be calculated using data from [44]. The compressibility of a helical head-to-tail chain formed by L-serine zwitter-ions in the structure of DL-serine is about 2.2 times higher, than that of a flat chain formed by the same L-serine zwitter-ions in the crystals of L-serine [37]. Further information can be obtained, if linear strain is considered with respect to the orientation of hydrogen-bonded layers. The structure of L-cystine is the most compressible in the direction normal to the hydrogen-bonded layers of zwitter-ions, in the direction of S-S bridges: changes in C-S-S-C torsion angles allow cystine molecules act like springs [42]. One could expect the structure of \( \alpha \)-glycine to be also the most compressible in the direction normal to the double layers, but it is not. The structure is about 1.2 times more compressible along the direction of hydrogen bonds linking the head-to-tail chains within a layer (Fig. 5) [24]. The structure of DL-serine is the most compressible in the direction, that forms about 30° with the normal to the double-layers, which approach each other with increasing pressure; this direction coincides with the direction of NH…O hydrogen bonds linking a double layer with another double layer, as well as with the orientation of the type II head-to-tail chains with alternating L- and D-serine zwitter-ions (Fig. 6). The structure is 5.2 times more compressible along this direction, than normal to it [37].

![Fig. 5 Orientation of the principal axes of the strain ellipsoid under pressure in \( \alpha \)-glycine; 1P – minimum, 3P – maximum compression, axis 2P is normal to the projection plane.](image-url)
Fig. 6. A fragment of the crystal structure of DL-serine as projected at (a x c)-plane at ambient conditions (a) and at 8.1 GPa (b). The orientation of the principal axes of strain tensor with increasing pressure (1P – slight expansion, 3P – maximum compression) is shown, axis 2P is normal to the projection plane [37].

2.3. Effect of pressure on the hydrogen bonds and other intermolecular contacts

Linear strain calculations can be complemented by the data on the shortening/stretching of hydrogen bonds with increasing pressure, if the structure is refined and coordinates of at least non-hydrogen atoms are known. Hydrogen bonds can be compressed or stretched with increasing pressure, and the change in the interatomic distance in a hydrogen bond does not always correlate with the value of linear strain of the crystal structure as a whole in the same direction, due to the conformational changes and rotation of molecules [25-30,66-68]. The compressibility of shorter NH…O hydrogen bonds linking zwitter-ions along the head-to-tail chains is usually smaller, than that of other hydrogen bonds in the structure [32,37,39,41-46]. It is only slightly affected even by jumpwise structural re-arrangements in the course of phase transitions. For example, in L-serine, the N-O distance in this hydrogen bond decreases practically linearly at about 0.01 Å / GPa in all the pressure range from ambient up to 10 GPa, although the crystal structure undergoes two phase transitions, at about 5 and at about 8 GPa, which are accompanied by a jump-wise increase in the cell parameter along the same head-to-tail chain (Fig. 7) [39]. The compressibility of the shorter NH…O hydrogen bonds in the head-to-tail chains remains almost unaffected by a structural arrangement of the triple helices formed by these chains in γ-glycine into a layer in δ-glycine in the course of the irreversible extended single-crystal – powder phase transition starting at about 3.5 GPa [31,32,36]. Other hydrogen bonds in the structures of crystalline amino acids are more compressible, than the short NH…O bonds within the head-to-tail chains, the changes in the N-O distances being usually about ± 0.02-0.05 Å / GPa [32,37,39,41-46]. Similar values were measured for the compressibility of NH…O and OH…O hydrogen bonds in other organic crystals [23,25-30,66-68]. For a comparison, recently measured typical values for proteins are about ± 0.1 – 0.01 Å / GPa [47,60-63]. One can analyze also the changes in other interatomic distances with pressure, for example, of the S-S intramolecular distances within a covalent bond and of the S-S intermolecular non-
covalent contacts in L-cystine [42], or of the CH$_2$…CH$_2$ contacts in the hydrophobic parts of the double layers present in many crystal structures of amino acids. Attempts were made even to correlate pressure-induced structural changes with the shortening of CH…O “hydrogen bonds” in the structures [41-46]. It is important to complete the analysis of geometrical parameters from diffraction data by spectroscopic experiments [69,70]. In some cases, spectroscopy does not confirm the presence of such interactions as hypothetic CH…O bonds, although the corresponding interatomic C-O distances meet the commonly accepted criteria [35,36,40,58,71,72].

Fig. 7. Cell parameters and volume versus pressure in the three polymorphs of L-serine [39]
2.4. Interrelation between the effect of pressure on the crystalline amino acids and on biopolymers

Analysis of the linear strain in crystalline amino acids, in particular – the analysis of the compressibility of selected structural elements (molecular chains, layers, intermolecular hydrogen bonds, “empty voids”), is important in relation to understanding the compressibilities of different structural fragments of peptides and proteins (helices, sheets, turns, non-structured fragments, cavities). For example, in some proteins, loops are more compressible, than helices, which, in turn, are more compressible, than β-sheets [47-49,59-62]. Compressibility of main chains can be compared with the strain in crystalline amino acids. This comparison should be expected to be more informative for fibrillar proteins, and for amiloid structures, than for globular proteins. While the globular native forms of proteins are side-dominated compact structures evolved by pursuing a unique fold with optimal packing of amino-acid residues, amyloid fibrils are a main-chain dominated structure, with an extensive hydrogen-bond network [12]. Pressure-induced phase transitions in crystalline amino acids, for example, the triple-helix to layer γ-glycine to δ-glycine pressure-induced transformation [31,32,36], can mimic conformational changes in amyloid structures and in fibrilar proteins like collagen [74]. Amyloids were recently shown to undergo pressure-induced structural transformations, during which contrasting conformational changes occur consecutively: first, a pressure-induced reorganization of fibrils, and then a pressure-induced unfolding [12]. The crystal structures of simple dipeptides can mimic those of the amyloid polypeptides [10], thus detailed high-pressure studies of these simpler systems could provide valuable information on the pressure effects on the amyloids themselves. It is very interesting also to compare the anisotropy of lattice strain in the crystals of amino acids with layered structures with the recently measured elastic properties of two-dimensional layers of oligopeptide films [75]. Compressibility of cavities of biopolymers, the contribution of the rigidity of the cavity to the conformational stability of the biopolymer can be also mimiced by studying structures of smaller molecules. Attempts were made to describe the anisotropic compression of some of the crystalline amino acids by “closing voids” [41-46]. Although, any pressure-induced process can be expected to result in a structure with a higher density and smaller voids, crystalline amino acids are still not the best systems to study compression of cavities, since their properties are to a large extent determined by dipole-dipole interactions and strong hydrogen bonds (OH…O and NH…O). Many of the crystals are piezoelectric, and this means, that pressure induces polarization, and noticeable electron density redistribution, that must be taken into account, when analyzing the anisotropy of pressure-induced structural strain and the mechanisms of phase transitions. Systematic comparative studies of series of amino acids – salts of amino acids – complexes of amino acids, in addition to the comparative studies of the polymorphs of the same amino acid and of the amino acids with different side chains, would be helpful. Much better mimetics for the “compressibility of cavities studies” can be selected among a family of dipeptides with nano-size cavities and channels, which have been extensively and carefully studied by C. Görbitz during the last decade [18,19]. One can compare the effect of pressure on layered dipeptides, and on the dipeptide crystal structures having large cavities of variable size and hydrophobic / hydrophilic properties. The same systems can be used to mimic the effect of liquids on the compressibility and the
conformational stability of the cavity. One can study compression in different liquids – hydrophilic, hydrophobic, containing special organic additives known to stabilize proteins of deep-sea piezophiles, using model crystal structures with the cavities of similar size, but with different – hydrophilic / hydrophobic – properties of the inner and outer walls of the cavities. Comparison of the compressibility values for different polymorphs (different structural arrangements of the same amino acids) and of the crystal structures of different amino acids may be relevant for understanding, why the fragments of proteins built by different sequences of amino acids compress differently. The knowledge of the elastic properties of the selected fragments of the amino acid crystals is needed when considering muscles, or biopolymers forming silk, or spider threads. One can also use the studies of strain induced by hydrostatic pressure, in order to understand better the conformational transitions induced by substrate-receptor interactions, by variations in temperature (cooling), or by collisions of the biopolymers. Varying side-chains, or the length of the main back-bone chains of amino acids and peptides forming the crystal structures, one can get control over dipole-dipole interactions, H-bond patterns, the occurrence / the absence of the inversion center, and then study the effect of the molecular arrangement on the mechanical properties in a very systematic way. Hydrates can be compared to anhydrous amino acids; salts – to amino acid molecules, mixed crystals with homomolecular phases, etc. Amino acids can be modified chemically, substituting protons for methyl-groups, in order to vary dipole-dipole interactions in a wide range. Selective deuteration can affect kinematic characteristics of zwitter-ions and H-bonding ability. Biomolecular assemblies (polyaminoacids, peptide two-dimensional layered or nano-porous structures) can serve as an important bridge between crystalline amino acids and proteins.

Phase transitions and polymorphism control in crystalline amino acids are related to the problem of folding of biopolymers, and of their stability with respect to pressure-induced conformational transitions, or denaturation (Table 1). A comparison of crystalline amino acids with dry fibrillar proteins, or with amiloid structures, which are extremely stable up to very high pressures [52], is especially relevant. Pressure-induced phase transitions in selected crystalline amino acids, such as L-alanine [22], or l-asparagine monohydrate [21] were observed by Raman spectroscopy already a long time ago, but only very recently diffraction data became available (for these and other systems), increasing enormously our potential in understanding the mechanisms of pressure-induced polymorphic transformations [31,32,38,39,41,43,45,46,76].

As an example, one can refer to the different response of the crystalline polymorphs of glycine to pressure. The structure of α-glycine (P2₁/n) is stable with respect to pressure-induced phase transitions at least up to 23 GPa [40], β-glycine (P₂₁) undergoes a reversible single-crystal to single-crystal phase transition at 0.76 GPa already [33,41], whereas γ-glycine (P₃₁) transforms irreversibly into δ-glycine (Pn) in a wide pressure range starting from about 3.5 GPa [31,32,41], which then converts into the ζ-form on decompression down to 0.6 GPa [36] (Fig. 8). The conclusion from the study of the pressure-induced phase transitions in the polymorphs of glycine is that they are controlled kinetically, so that not the same state is obtained at the same P-T conditions, depending on the starting structure. An important observation was that the head-to-tail chains of zwitter-ions are preserved, whatever happens to the crystal structure, also during the phase transitions. A transformation from a triple-helix structure into a layered structure is possible, but is irreversible. Transitions between
different non-centrosymmetric layered structures are possible, double centrosymmetric layers are extremely stable. These findings may be relevant for the problem of different conformational stability of the regions of the peptides differing in secondary structure, for example—of α-helices, and β-sheets, as well as to understanding the mechanism of triple-helix to layer conformational transitions in collagens and other fibrillar proteins [74].

![Fig. 8. Fragments of the crystal structures of \(\gamma\)-glycine (a) and \(\delta\)-glycine (b) [31,32].](image)

Pressure-induced isosymmetric single-crystal to single-crystal phase transitions in L-serine provide another example, illustrating the role of conformational flexibility of an amino acid in the transformations [35,38,39,43,46]. In contrast to glycine, serine zwitter-ions show significant jump-wise changes in the conformations with increasing pressure (some torsion angles change at about 22 degrees); reversible phase transitions are related to jump-wise changes in hydrogen bond networks; two-dimensional layers expand and get flatter, resulting in total volume decrease with increasing pressure (Fig. 9) [39]. Large conformational changes were observed also during pressure-induced phase transitions in L-cysteine [45]. It is worthy noting, that it is the large conformational flexibility of L-serine, that makes this residue so important for the substrate-receptor recognition and for the mechanical functions and cell motility in many biochemical processes [77-84]. Cascade-type cooperative phase transitions in L-serine with a rapidly propagating interface can be compared with conformational changes responsible for the functioning of serine zippers in biochemical systems [85,86].
The values of bulk compressibilities, and the V(P) dependencies do not allow one to predict the stability of a structure with respect to pressure-induced phase transitions. For example, although L- and DL-serine have very similar bulk compressibilities up to about 5 GPa, the ambient-pressure phase of DL-serine remains stable, at least, up to 8.6 GPa, whereas L-serine undergoes two isosymmetric phase transitions – at about 5 GPa, and at about 8 GPa [34,35,37-39,43,46]. Less-compressible L-cystine [42], and more compressible $\alpha$-glycine, and $\alpha$-glycylglycine show no phase transitions, at least up to 6.4 GPa [42], 23 GPa [40], 6 GPa [71], respectively. Pressure induces phase transitions in a low-compressible $\gamma$-glycine [24,31,32,36], middle-compressible L-serine [35,38,39,43,46], and highly compressible L-cysteine [45].

3. Conclusion

Summing up, the studies of crystalline amino acids at high pressures are still in the very initial stage; dipeptides remain practically unstudied, with $\alpha$-glycylglycine as the only exception. At the same time, the knowledge of the details of the structural response of the crystalline amino acids to the variations in pressure can provide interesting information relevant to understanding the high-pressure behavior of biopolymers.
4. References


[78] Hepler, P.K. Cell motility and the cytoskeleton; unconventional myosins, Biology 574; Fall 2000 (http://www.bio.umass.edu/vidali/web/cell_motil/oct_3_long1.htm)


5. Acknowledgement

The review is based mainly on the experimental results obtained by the author in collaboration with Dr. H. Sowa, Dr. H. Ahsbahs, Dr. H. Uchtmann, Dr. S.V. Goryainov, Dr. Yu.V. Seryotkin, Dr. S.N. Ivashevskaya, Dr. V.V. Chernyshev, Dr. E.B. Burgina, Dr. T.N. Drebushchak, Dr. V.P. Dmitriev, Dr. H.-P. Weber, E.N. Kolesnik. Financial support was received from various Foundations and Programs, such as DFG, DLR, Humboldt Foundation, RFBR, CRDF (BRHE Program), Russian Ministry of Education and Science, Multidisciplinary integration projects from the SB RAS. Experiments using synchrotron radiation were performed at SNBL station of the ESRF (Grenoble, France). Experiments under laboratory conditions were carried out partly in Marburg (Germany), and partly in Novosibirsk (Russia).