N E W S
OF THE NATIONAL ACADEMY OF SCIENCES OF THE REPUBLIC OF KAZAKHSTAN
PHYSICO-MATHEMATICAL SERIES
ISSN 1991-346X
Volume 2, Number 312 (2017), 5 – 9

UDC 548.735+548.31+577.112.387.2+ 577.112.37+661.8...35

S.B. Berdibay[1,2,*], N.A. Paretskaya[2], A.N. Sabitov[2], R.A. Islamov[2], R.A. Tamazyan[3], S.Zh. Tokmoldin[1], A.I. Ilin[2], K.S. Martirosyan[4]

[1]K.I. Satpayev Kazakh National Research Technical University, Almaty, Kazakhstan;
[2]Scientific Center for Anti-Infectious Drugs, Almaty, Kazakhstan;
[3]The foundation "Research Center for Advanced Technologies", Yerevan, Armenia;
[4]The University of Texas Rio Grande Valley, Texas, USA
*E-mail: sniper_8888@mail.ru

PHENYLALANINE – IODINE COMPLEX AND ITS STRUCTURE

Abstract. This report describes synthesis and structural characterization of the phenylalanine·iodine complex monocrystal in acetone. Crystals of the substance exhibited a rhombic syngony and were stable at a temperature of 25 °C. As a result, a new compound α,α'-di-amino-β,β'-diphenylpropionic acid monoiodide has been obtained. X-ray diffraction analysis showed that dimers of phenylalanine molecules ($C_{18}H_{23}N_2O_4$) are formed due to hydrogen bonds between the oxygen atoms of carboxyl groups. The hydrogen bonds between the amino groups and iodide form the layers parallel to the (001) plane and these molecular layers are bound to a three-dimensional structure via the van der Waals forces.

Keywords: Phenylalanine, iodine, halogen, hydrogen bonds, amino acid complex with iodine.

Introduction

Iodine, in comparison with other halogens - fluorine, chlorine and bromine, has a number of distinctive properties. First of all, the interatomic distance in the iodine molecule in the solid state is greater than in the gaseous state. This is not observed in either chlorine or bromine. Due to the large size of the iodide anion, the iodide has a small surface charge density, as a result of which the charge distribution can be distorted by the action of certain cations (Li^+, Mg^{2+}, Fe^{3+}, etc.) and can no longer be regarded as spherically symmetric [1]. In comparison with chlorine and bromine, high iodine polarizability along with low electronegativity makes it possible to form various compounds like charge transfer, donor-acceptor interaction, hydrophobic interaction, hydrogen and halogen bonds [2,3]. These properties of iodine enable to develop a variety of substances and materials, for example, drugs [2], superconductors [4], nonlinear optical crystals [5]. Iodine forms complex compounds with organic substances and interhalogen compounds, including polyiodides [6-9]. Of particular interest are the compounds of iodine with amino acids [10]. The aim of the study was a synthesis of a complex of phenylalanine and iodine and determination its structure by X-ray diffraction analysis.

Experimental part

Synthesis of the phenylalanine·iodine complex. Acetone (Sigma, USA) and iodine (Reachim, Russia) were mixed in a molar ratio of 34:1 at a temperature of 60-65°C to produce hydrogen iodide:

$$H_3CCOCH_3 + I_2 \rightarrow CH_2ICOCH_3 + HI \quad (1)$$

Then phenylalanine was added and acetone was slowly evaporated. As the acetone evaporates, crystals of black color form for a long time. The obtained crystals had a rhombic syngony and were stable

at a temperature of 25°C. The chemical formula of this compound can be represented as: $2C_9H_{11}NO_2 \cdot HI$, and the formation reaction:

$$2C_9H_{11}NO_2 + HI \rightarrow [H(C_9H_{11}NO_2)_2I] \quad (2)$$

X-ray diffraction analysis (XRD). A single-crystal needle-shaped sample of 0.02 x 0.08 x 0.28 mm in size was placed in a glass capillary and fixed with a glass rod. To prevent the destruction of crystals under the influence of heat and X-rays, diffraction measurements were carried out at low temperatures. Low temperatures on the samples were maintained by a low temperature prefix of the "Enraf-Nonius" firm in pairs of nitrogen with an accuracy of ±1°C. Diffraction measurements were carried out at room temperature on an Enraf-Nonius CAD-4 auto-diffractometer (graphite monochromator, Mo-K_α radiation, $\theta/2\theta$- scanning). The parameters of the rhombic cell are determined and refined by 24 reflections with $12<\theta<13$. The absorption was accounted for using the psi-scan method [11]. The structure is deciphered by the direct method. The coordinates of all hydrogen atoms are determined by geometric calculations. The structure is defined by the completely matrix OLS in the anisotropic approximation for non-hydrogen atoms and isotropic for hydrogen atoms. The coordinates of the hydrogen atoms of the NH_3 and OH groups are refined freely, and the coordinates of the remaining hydrogen atoms are refined by the "rider" model with the following conditions: the length of the bonds is C-H=0.98Å, 0.97Å, 0.93Å and $U_{iso}(H)=1.5U_{eq}(C)$ for CH, CH_2 and phenyl groups, respectively. All structural calculations were carried out using the SHELXTL program complex [12].

The main crystallographic data and experimental parameters are given in Table 1, and the full crystallographic information of the investigated compound was deposited at the Cambridge structural data bank under the number CCDC 1036670.

Table 1 - Crystallographic data of the complex $2(C_9H_{11}NO_2) \cdot HI$

Formula	$2(C_9H_{11}NO_2) \cdot HI$
Molecular weight	458.28
Singonia; Spatial group	Rhombic; $P2_12_12_1$
Lattice parameters a, b, c [A]	5.3059(11);12.265(3); 29.585(6)
alpha, beta, gamma [deg]	90.0; 90.0; 90.0
V $[A]^3$; Z	1925.3(7); 4
D(calc)[g/cm^3]; F(000)	1.581; 920
Mu(MoKa) [mm^{-1}]	1.687
Dimensions of the crystal [mm]	0.02 x 0.08 x 0.28
Измерения	
Temperature (K); Radiation [A]	200; MoKa; λ=0.71073
6min;6max[Deg]	1.4, 30.0
Measurement area	0: 7;-17: 17; 0:41
Number of reflexes changed, independent, R(int)	6498, 5612, 0.048
Observed reflexes [I>2.0 sigma(I)]	3154
Refinement	
Number of reflexes, Number of parameters	5612, 247
R, wR^2, S	0.0616, 0.1304, 0.81
Max. and Av. Shift/Error	0.00, 0.00
Flack x	0.00(4)
Min. and Max. Resd. Dens. [e/A^3]	-0.69, 0.85

Results and discussion

The structure of the complex $2(C_9H_{11}NO_2) \cdot HI$, determined by X-ray diffraction analysis, is shown in Fig. 1. The independent part of the unit cell contains two molecules of phenylalanine ($C_9H_{11}NO_2$), and one anion I^-.

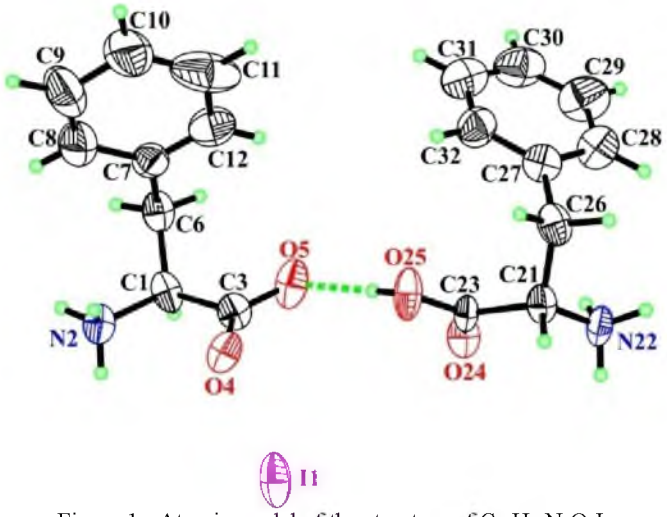

Figure 1 - Atomic model of the structure of $C_{18}H_{23}N_2O_4I$
(ellipsoids of anisotropic thermal oscillations are drawn at the level of 50% probability)

Herewith, two molecules of phenylalanine are bound by the hydrogen bond O25-H25···O5 (Table 2) to form a dimer ($C_{18}H_{23}N_2O_4$) (Figure 1).

Table 2 - Hydrogen bonds in structure $2(C_9H_{11}NO_2)\cdot HI$

D	H	A	D-H	H-A	D-A	D-H-A
N2	H2A	O24	0.92(4)	1.87(4)	2.778(7)	168(5)
N2	H2B	I1	0.92(7)	2.81(8)	3.642(6)	151(7)
N2	H2C	I1	0.92(8)	2.79(8)	3.575(6)	144(8)
N22	H22B	O4	0.93(4)	1.83(4)	2.760(7)	173(3)
N22	H22A	I1	0.93(8)	2.77(8)	3.602(6)	149(7)
N22	H22C	I1	0.93(6)	2.75(8)	3.616(6)	158(7)
O25	H25	O5	0.88(9)	1.66(9)	2.423(6)	144(8)

In the three-dimensional packaging of the crystal structure, the dimers ($C_{18}H_{23}N_2O_4$) form an infinite two-dimensional layer parallel to the plane (001) due to the hydrogen bonds between the amino groups and iodide (Figure 2). In the three-dimensional construction of the crystal structure, the interaction between the layers is mainly described by van der Waals forces.

Thus, in the reaction of iodine with phenylalanine in acetone, a complex α,α'-di-amino-β,β'-diphenylpropionic acid monoiodide is formed. Iodine atoms are the acceptors of the hydrogen bond formed with amino groups of phenylalanines of the type:

$$N - H\cdots X^-$$

where, X = F, Cl, Br и I

The average and normalized length of the hydrogen bond H...X- is 0.83 and, being less than the mean value 0.873 [13], calculated from known structures, indicates a strong hydrogen bond.

The obtained complex differs from other coordination compounds of iodine with amino acids [10] or other biologically active substances [14] with charge transfer by type:

$$n*\text{Amino acid} + I_2 + KI \rightarrow [(\text{Amino acid})_nK]^+\cdot I_3^- \quad (3)$$

where, $n \geq 1$

Iodide promotes the dimerization of phenylalanines, initiating the formation of the hydrogen bond between pairs of amino acid molecules. As it is known, multidimensional structures, formed by hydrogen bonds between biological molecules, play an important role - from metabolic transformations to the realization of genetic information encoded in DNA [15, 16]. The role of halogen ions in the stabilization of the action of the reactive center of enzymes is great. For example, the chlorine anion activates the α-

amylase of animals and certain bacteria by forming the hydrogen bond with the amino group of arginine [17]. Similarly, chloride affects cathepsin C [18]. Therefore, interest in halogens as acceptors of the hydrogen bond is very high.

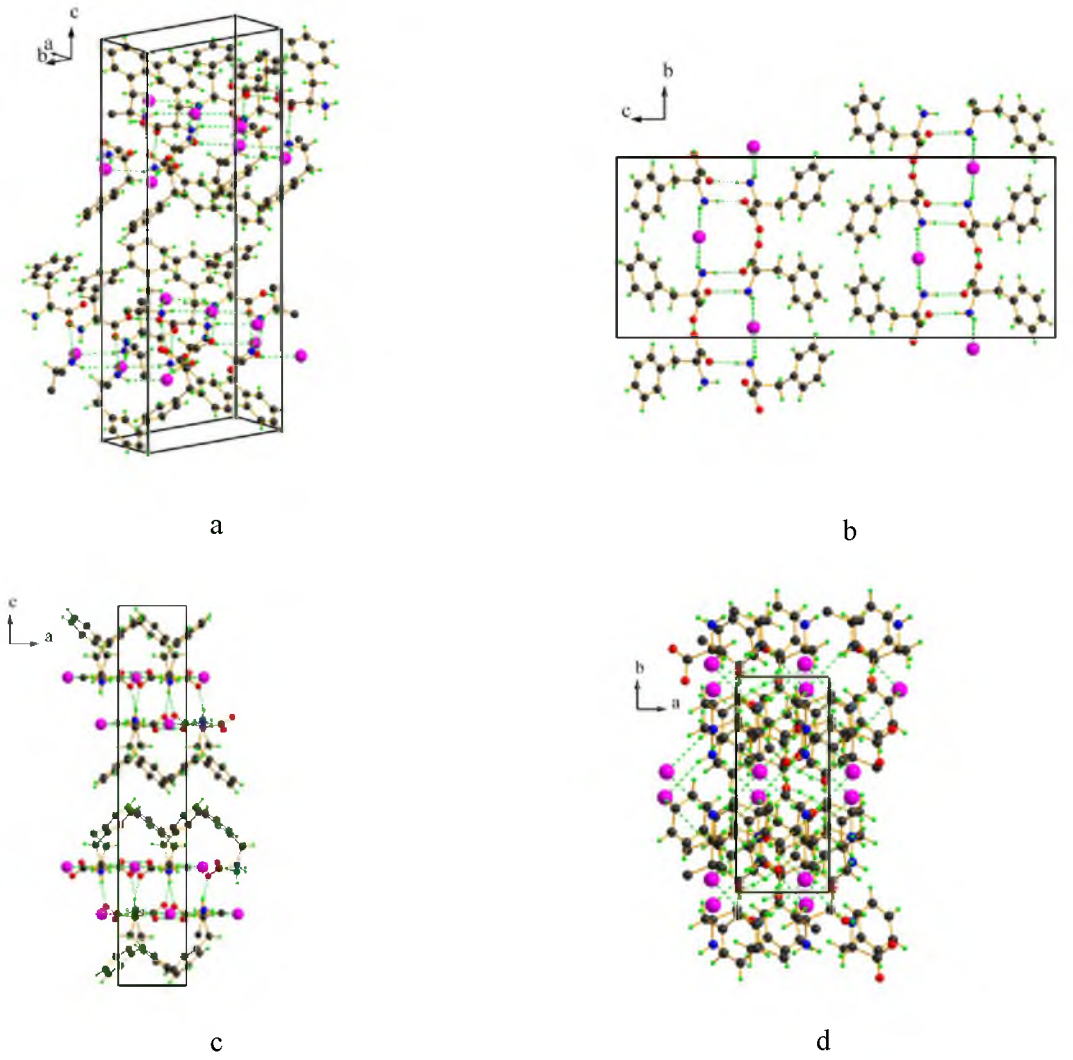

Figure 2 - Crystalline structure $C_{18}H_{23}N_2O_4I$, iodine atoms of magenta colour, carbon - gray, nitrogen - blue, oxygen - red and hydrogen - green, hydrogen bonds are shown in green broken lines: (a) - a perspective view of the structure; (b) - the projection of the structure on (100); (c) - the projection of the structure on (010); (d) - the projection of the structure on (001)

REFERENCES

[1] Hauskroft K, Konstebl Je. (2002) Sovremennyj kurs obshhej himii. Mir, Rossija. ISBN 5-03-003310-6. (In Russian)

[2] Kupper FC, Feiters MC, Olofsson B, Kaiho T, Yanagida S, Zimmermann MB, Carpenter LJ, Luther GW 3rd, Lu Z, Jonsson M, Kloo L. (2011) Commemorating two centuries of iodine research: an interdisciplinary overview of current research, Angew Chem Int Ed Engl, 50:11598-11620. DOI: 10.1002/anie.201100028

[3] Bartashevich EV, Cirel'son VG. (2014) Vzaimnoe vlijanie nekovalentnyh vzaimodejstvij v kompleksah i kristallah s galogennymi svjazjami, Uspehi himii, 83:1181-1203. DOI: 10/RCR4440. (In Russian)

[4] Mihalache V, Aldica GV, Miu D. (2007) Superconducting properties of iodine-intercalated Bi2Sr2Ca2Cu3O10+x, J Supercond Nov Magn, 20:261-272. DOI: 10.1007/s10948-006-0199-y

[5] Yin Z, Wang QX, Zeng MH. (2012) Iodine release and recovery influence of polyiodide anions on electrical conductivity and nonlinear optical activity in an interdigitated and interpenetrated bipillared-bilayer metal-organic framework, J Am Chem Soc, 134:4857-4863. DOI: 10.1021/ja211381e

[6] Refat MS, Al Didamony H, Abou El-Nour KM, El-Zayat L. (2010) Synthesis and spectroscopic characterization on the tri-iodide charge transfer complex resulted from the interaction between morpholine as donor and iodine sigma-acceptor, J Saudi Chem Soc, 14:232-330. DOI: 10.1016/j.jscs.2010.04.004

[7] Blake AJ, Li WS, Lippolis V, Parsons S, Schröder M. (2007) Extended structures of polyiodide salts of transition metal macrocyclic complexes, Acta Crystallogr B, 63:81-92. DOI: 10.1107/S0108768106041668

[8] Walbaum C, Pantenburg I, Junk P, Deacon GB, Meyer G. (2010) Bulky Cations and Four different Polyiodide Anions in [Lu(Db18c6)(H2O)3(thf)6]4(I3)2(I5)6(I8)(I12), Z Anorg Allg Chem, 636:1444-1446. DOI: 10.1002/zaac.201000112
[9] Madhu S, Evans HA, Doan-Nguyen VV, Labram JG, Wu G, Chabinyc ML, Seshadri R, Wudl F. (2016) Infinite polyiodide chains in the pyrroloperylene-iodine complex: insights into the starch-iodine and perylene-iodine complexes, Angew Chem Int Ed Engl, 55:8032-8035. DOI: 10.1002/anie.201601585
[10] Mahmoud KR, Refat MS, Sharshar T, Adam MA, Manaaa El-SA. (2016) Synthesis of amino acid iodine charge transfer complexes in situ methanolic medium: Chemical and physical investigations, J Mol Liq, 222:1061-1067. DOI: 10.1016/j.molliq.2016.07.138
[11] North ACT, Phillips DC, Mathews FS. (1968) A Acta Cryst, A24:351-359.
[12] Sheldrick GM. (2008) All programs beginning with SHELX, Acta Cryst, A64:112-122
[13] Brammer L, Bruton EA, Sherwood P. (2001) Understanding the behavior of halogens as hydrogen bond acceptors, Crystal Growth & Design, 1:277-290. DOI: 10.1021/cg015522k
[14] Solanki GK, Amin A, Padhiyar A, Ray AK, Oza AT. (2008) Polaron hopping in some biomolecular solids and their charge transfer complexes, Indian J Biochem Biophys, 45:421-429
[15] Bissantz C, Kuhn B, Stahl M. (2010) A Medicinal Chemist's Guide to Molecular Interactions, J Med Chem, 53:5061-5084. DOI: 10.1021/jm100112j
[16] Scholfield MR, Zanden CMV, Carter M, Ho PS. (2013) Halogen bonding (X-bonding): A biological perspective, Protein Sci, 22:139-152. DOI: 10.1002/pro.2201
[17] Aghajari N, Feller G, Gerday C, Haser R. (2002) Structural basis of α-amylase activation by chloride, Protein Sci, 11:1435-1441. DOI: 10.1110/ps.0202602
[18] Cigic B, Pain RH. (1999) Location of the binding site for chloride ion activation of cathepsin C, Eur J Biochem, 264:944-951

ӘОЖ: 548.735+548.31+577.112.387.2+ 577.112.37+661.8...35

С.Б. Бердібай[1,2], Н.А. Парецкая[2], А.Н. Сабитов[2], Р.А. Исламов[2], Р.А. Тамазян[3], С.Ж. Токмолдин[1], А.И. Ильин[2], К.С. Мартиросян[4]

[1]Қ.И. Сәтбаев атындағы Қазақ Ұлттық техникалық зерттеу университеті, Алматы қ., Қазақстан;
[2]Инфекцияға қарсы препараттар ғылыми орталығы, Алматы қ., Қазақстан;
[3]Перспективалық технологиялар зерттеу орталығы фонды, Ереван қ., Армения;
[4]The University of Texas Rio Grande Valley, Texas, USA

ИОД ЖӘНЕ ОНЫҢ ҚҰРЫЛЫМЫМЕН ФЕНИЛАЛАЛИННІҢ КЕШЕНДІ КОМПЛЕКСІ

Аннотация. Мақалада ацетонда фенилаланин-иод кешенінің монокристаллды алу және синтезі сипатталады. Заттың кристалы ромбылық сингониясы болды және 25 °С температурада тұрақты болды. Нәтижесінде α,α'-ди-амино-β,β'-моноиодид дифенилпропионды қышқылының жаңа қосылысы алынды. Рентгендік құрылымдық зерттеулерімен фенилаланиннің молекула диметрлері ($C_{18}H_{23}N_2O_4$) карбоксил топтарының оттегі атомдар арасындағы сутектік байланыс салдарынан пайда болатынын көрсетті. Амин топтары мен иодид арасындағы сутектік байланыс параллель жазықтық қатпары пайда болып, осы молекулалар қатпарлары Ван-дер-Ваальс арқылы үш өлшемді құрылысын байланыстырады.

Түйін сөздер: фенилаланин, иод, галоген, сутектік байланыстар, иодпен амин қышқылы кешені.

УДК 548.735+548.31+577.112.387.2+ 577.112.37+661.8...35

С.Б. Бердібай[1,2,*], Н.А. Парецкая[2], А.Н. Сабитов[2], Р.А. Исламов[2], Р.А.Тамазян[3], С.Ж. Токмолдин[1], А.И. Ильин[2], К.С. Мартиросян[4]

[1]Казахский национальный исследовательский технический университет им. К.И. Сатпаева, Алматы, Казахстан;
[2]Научный центр противоинфекционных препаратов, Алматы, Казахстан;
[3]Фонд «Центр исследования перспективных технологий», Ереван, Армения;
[4]The University of Texas Rio Grande Valley, USA

КОМПЛЕКС ФЕНИЛАЛАНИНА С ИОДОМ И ЕГО СТРУКТУРА

Аннотация. В статье описывается синтез и структурный анализ монокристалла комплекса фенилала-нин·иод в ацетоне. Кристаллы вещества имели ромбическую сингонию и были стабильны при температуре 25 °С. В результате получено новое соединение α,α'-ди-амино-β,β'-дифенилпропионовой кислоты моноиодид. Рентгенрструктурными исследованиями показано, что димеры молекул фенилаланина ($C_{18}H_{23}N_2O_4$) образуются за счёт водородных связей между атомами кислорода карбоксильных групп. Водородные связи между аминогруппами и иодидом образуют слои параллельно плоскости (001) и эти слои молекул связываются в трехмерную постройку силами Ван-дер-Ваальса.

Ключевые слова. Фенилаланин, иод, галоген, водородные связи, комплекс аминокислоты с иодом.