ЕҢБЕК ҚЫЗЫЛ ТУ ОРДЕНДІ
«Ә. Б. БЕКТҰРОВ АТЫНДАҒЫ
ХИМИЯ ҒЫЛЫМДАРЫ ИНСТИТУТЫ»
АКЦИОНЕРЛІК ҚОҒАМЫ

ҚАЗАҚСТАННЫҢ ХИМИЯ ЖУРНАЛЫ

ХИМИЧЕСКИЙ ЖУРНАЛ КАЗАХСТАНА

CHEMICAL JOURNAL of KAZAKHSTAN

АКЦИОНЕРНОЕ ОБЩЕСТВО
ОРДЕНА ТРУДОВОГО КРАСНОГО ЗНАМЕНИ
«ИНСТИТУТ ХИМИЧЕСКИХ НАУК
им. А. Б. БЕКТУРОВА»

3 (63)

ИЮЛЬ – СЕНТЯБРЬ 2018 г.

ИЗДАЕТСЯ С ОКТЯБРЯ 2003 ГОДА

ВЫХОДИТ 4 РАЗА В ГОД

АЛМАТЫ
2018

UDC 539.2+577.1+541.49

A. B. IBRAGIMOV[1], L. MAMASALIEVA[1], R. KIM[1], O. MYACHINA[1], B. S. ZAKIROV[1], B. T. IBRAGIMOV[2], J. M. ASHUROV[2], A. A. MAMADRAHIMOV[2]

[1]Institute of General and Inorganic Chemistry of Uzbekistan Academy of Sciences, Tashkent, Republic of Uzbekistan,
[2]A.Sadykov Institute of Bioorganic Chemistry of Uzbekistan Academy of Sciences, Tashkent, Republic of Uzbekistan

STRUCTURE AND BIOLOGICAL ACTIVITY OF THE MIXED-LIGAND COMPLEX OF COPPER WITH P-NITROBENZOIC ACID AND MONOETHANOLAMINE

Abstract. Analysis of the current state of theory and practice of various growth stimulants application allows to note their wide use in agriculture, where they play important role such as mineral fertilizers. In this connection, a lot of number growth stimulants are created, and compounds based on metal complexes take important place.

Key words: p-nitrobenzoic acid, monoethanolamine, Cu complex, molecular and crystal structure, SAR, TG-DSK, mass spectrum, growth stimulating activity.

Introduction. The possibility of an enhancement of biological action of the low-active organic substances by formation of monoligand metal complexes was studied in detail, and very promising results were obtained [1-3]. However, the literature analysis indicates that there are no works devoted to systematic study of bioactivity optimization in mixed-ligand complexes.

Very promising is the approach when cheap and commercially available substances demonstrating simultaneous antimicrobial and growth-stimulating actions will be used as the main ligand. The simplest mono-derivatives of benzoic acid, as nitro-, amino- and hydroxybenzoic acids are such compounds [4]. Ethanolamines, showing the same biological effect can be selected as an auxiliary ligand [5]. Based on this, we conducted the syntheses with participation of the p-nitrobenzoic acid (PNBA), monoethanolamine (MEA) and salt of copper (I) sulfate (Cu_2SO_4) salt.

Thus we have synthesized a new mixed-ligand metal complex of copper containing two molecules of PNBA and two molecules of MEA.

EXPERIMENTAL PART

A hot solution of PNBA containing 0.167 g (1 mmol) in methanol was added to solution of water-methanol mixture (1: 0.25 by volume) containing 0.135 g (0.5 mmol) of $CuCl_2 \cdot 2H_2O$ in 4 ml. In to this mixture 62 μl of MEA was added dropwise with constant stirring. The reaction mixture was kept in an ultrasonic bath (30 kHz) for 10 minutes. The resulting solution was placed in a tub, not tightly closed (at 20° C). After 8 days prismatic crystals are formed. The yield was about 60%.

Experimental data for X-ray diffraction analysis were collected using the CrysAlisPro program [6] on an X-ray difractometer "Xcalibur R CCD" (Oxford diffraction, England) using CuK_α radiation with λ=1.5418Å (graphite monochromator, ω-scanning method). The correction for absorption was made by a multi-scan method of the same program. The structures were solved by a direct method and refined by the least square method [7] using the SHELXS-97 software packages [8]. Molecular and crystalline structures were plotted by the MERCURY software [9]. The crystallographic parameters and details of structure refinement are given in the table 1.

Table 1 – Crystallographic parameters and details of the structure refinement of the mononuclear mixed-ligand Cu complex.

Characteristics	Amount of parameters value of quantity
Formula	$Cu[((PNBA)_2+(MEA)_2)]$
Crystal system	Monoclinic
Etc. gr.	$P2_1/n$
a, Å	4.781(5)
b, Å	21.252(5)
c,Å	10.701(5)
α, deg	90
β, deg	97.375(5)
γ, deg	90
V, $Å^3$	1078.3(13)
Z	2
ρ(calculated), g / cm^3	1.595
μ, mm^{-1}	1.077
Crystal dimensions, mm	0.08 x 0.16 x 0.40
Scanning interval θ, deg	3.9, 50.2
h, k, l range	-5:5; -25:24; -11:12
Collected reflections	7618
R_{int}	0.034
Reflections with $I > 2\sigma (I)$	1540
GOOF (F2)	1.08
R1, wR2 (I> 2σ (I))	0.0601, 0.1956
$\Delta\rho_{max}$, $\Delta\rho_{min}$, e / $Å^3$	-0.56, 0.48

The thermal analysis of compounds was carried out in an inert argon atmosphere under programmable non-isothermal heating conditions in mixture with α-Al_2O_3 standard in ratio 1: 1 at heating rate of 10 deg / min in 25-400°C temperature interval on combined thermal analyzer STA 409 PC LUXX from Netzsch (Germany). Mass spectra were registered using an ion trap mass spectrometer and time-of-flight mass spectrometer Aglient 6400 TripleQuadrupole LC / MS (Germany) and Q-TOF Agilent 6520 va 6400 TripleQuadrupole LC / MS (Germany), respectively. The ionization was performed by electrospray, the mass spectra were recorded with the following experiment parameters: m / z range 50-400, dehydration gase flow rate (nitrogen) 3 ml / min at 300 ° C, gas pressure on nozzle needle 20 psi , the voltage of the fragmentator is 35 V, capillary voltage is 3500 V.

Results and Discussion. In the crystals, the Cu^{2+} ions located at inversion centers are coordinated chelatly by two MEA molecules through nitrogen and oxygen atoms (figure 1). Two more PNBA molecules are monodentately attached to metal ions, both by oxygen atoms of the carboxyl group, which is in carboxylate form in order to compensate positive charge of the copper ions. The carboxylate group is not coplanar with benzene ring - the corresponding dihedral angle is 25.28 °. The nitro group is inclined to aromatic nucleus at 11.51º.

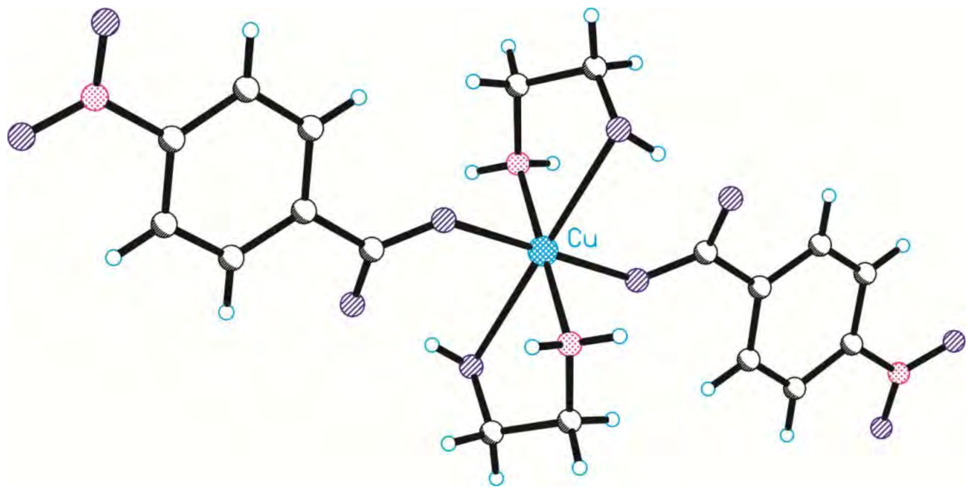

Figure 1 – The structure of the complex molecule in the Cu[($(PNBA)_2$+$(MEA)_2$)] compound

Polyhedron of the copper ions is octahedron which is strongly distorted by the Jahn-Teller effect [10-12].

The mixed ligand metal complex with composition of Cu [($(PNBA)_2$+ $(MEA)_2$)] is stable up to 167°C (figure 2) and loss of mass in the temperature range of 20-370 ° C occurs in one stage - 167-320° C, in this interval the thermal decomposition of the sample with loss of weight of 62.16% takes place. The DSC-curves show two peaks: endothermic - T_{max} 155.2 and the immediately

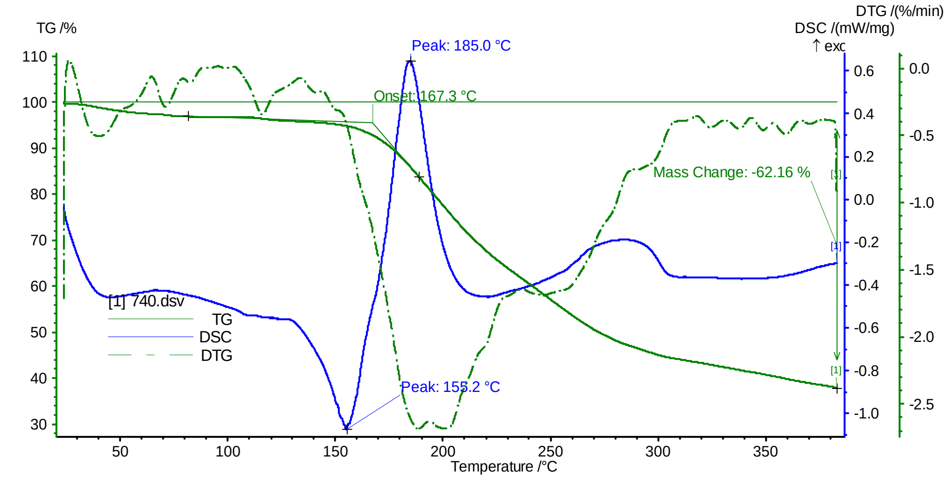

Figure 2 – Thermal analysis of the complex Cu[((PNBA)$_2$+ (MEA)$_2$)]

following exothermic peak at T_{max} 185 ° C. The first peak corresponds to sample melting, and the subsequent thermal oxidative destruction is characterized by an exothermic peak. The total amount of energy corresponding to these processes is 157 J / g. The maximum degradation rate is 2.5% per minute.

To study the component composition, the complex compounds were analyzed by HPLC-mass spectrometry (figure 3). After the scan with positive ionization, a molecular fragments with the characteristics [M + H] = 518, [M = 517 + 1] were detected, and it can be assumed to formation of the complex, which is sufficiently resistant to external influences.

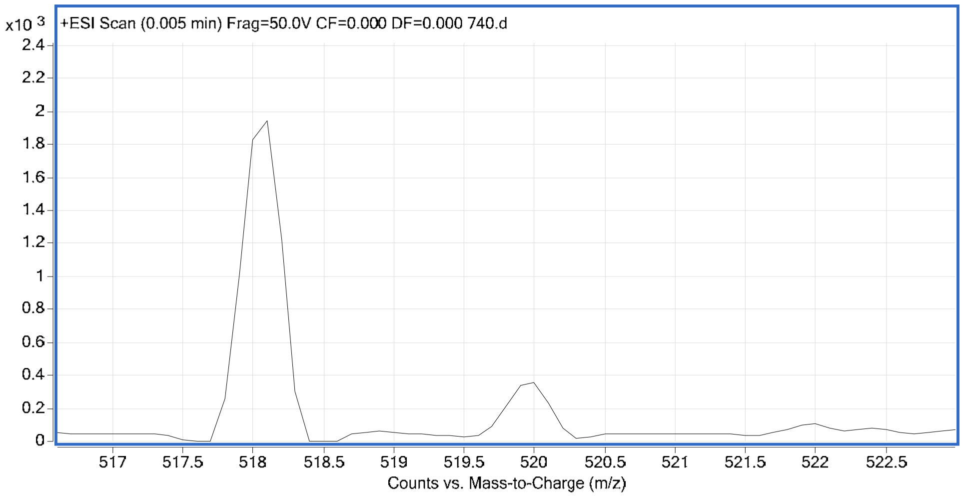

Figure 3 – Mass spectrometry of the complex Cu[((PNBA)$_2$+ (MEA)$_2$)]

Thus, the $Cu[((PNBA)_2+(MEA)_2)]$ compound is a mixed-ligand mononuclear complex of Cu (II) with PNBA and MEA of 1: 2: 2 ratio.

Growth stimulating activity. PNBA shows growth stimulating activity, but significantly less than *p*-aminobenzoic acid [13]. The stimulating effect of MEA is much greater, and therefore preparations based on this substance are used as growth stimulants [14]. In this connection, synthesized compounds should exhibit enhanced growth-stimulating properties.

During the experiments, the testing compound - mononuclear complex of Cu with PNBA and MEA was designated as substance No.1.

In vegetative experiments, the effect of synthesized compound on the growth, development, and harvest of cotton-wool was studied. Before sowing, the seeds were soaked with water and tested stimulants with 0.001% concentration. In the growing phase of 3-4 true leaves, in the budding and flowering - fruit-formation phases of cotton growing, the plants were sprayed with the test preparation [15, 16].

When applying the plant growth stimulator, the general provisions are observance all rules of agricultural technology, support of good plant nutrition regime, and observing the rules for using the stimulant so as not to destroy the plant. The growth stimulator was stored in tightly closed glass container with plug glass stopper in dry and dark place or in opaque containers.

During the cotton growing period, careful maintenance of plants was carried out: watering, loosening of the soil, thinning, fertilizing, treatment of plants from diseases, phenological observations and biometric measurements were carried out. During the growing season, soil moisture was maintained at 60-65% of total moisture capacity.

The vegetation experience was carried out in 4-fold replication.

Soil under the experience: typical serozem (Calcisol, WRB, 2006) with the following characteristics: C_{total} - 0.54%; N_{total} - 0.09%; P_{total} - 0.14%; pH 7.2.

The stimulator was studied on cotton crop (*Gossypium hirsutum*) of the "Akdarya-6" sort in vegetation experiments. The average vegetative period of plants varies from 117 to 128 days.

The land treatments were carried out according to generally accepted technique of Cotton Breeding, Seed Production and Agro-Technologies Research Institute (Tashkent, Uzbekistan).

In the experiments special attention was paid to acceleration of development rates of cotton- plants. In Fig. 4 the influence of studied stimulator on growth of main cotton-plants stem on different development stages is clearly traced. If in germination stage there was no significant difference in variants, then stimulating effect of studied complex on plant growth is found to phase of 3-5 true leaves (the length of the main stem is 61.3% longer than in control version). The highest plants are fixed in variant with stimulator, reaching a maximum of 18.0 cm, which exceeds the control variant by 6 cm (i.e. by 50%). In the flowering phase and in terminal stage of fruit formation (maturation), the intensification of plants growth was noted: in the stimulator variant the length of plant main stem were

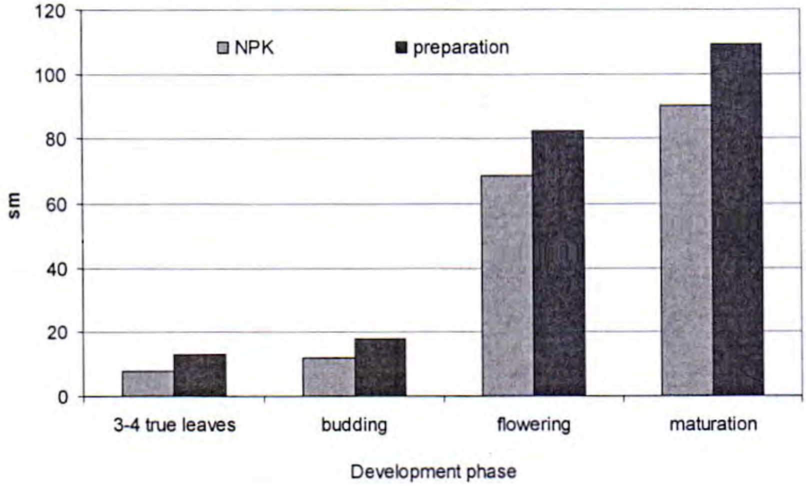

Figure 4 – Dynamics of cotton growth under the influence of the preparation

respectively 82.25 and 109.25 cm (which is 19.6 and 21.1% longer than in control).

The main criterion which make for effectiveness of studied preparation is the level of cotton-wool harvest. From the results presented in table. 2. it can be seen that the yield of in the test group of plants (with growth stimulator) was 28.3% higher than yield from the control plants (without stimulant). It is important that under influence of mixed-ligand complex, the opening and ripening of bolls is somewhat delayed. Thus, in the control variant 70% of cotton-wool was collect at first harvest, while in tested variant only 45.7%, for 2 harvest, respectively, 20.0 and 30.1%, for 3 harvest - 9.4 and 24.1% of the total harvest of cotton-wool.

It should be especially noted that in variant with mixed ligand complex, in addition to increasing bolls number from one plant (up to 33.75 pcs vs. 26.0 pcs in control, i.e. by 29.8% more), the complete ripening of formed bolls was fixed (the number of unripe fruit-elements in test variant was 41.5% less: 11.3 pieces versus 19.3 in the control). These phenomena together contributed to increase in yield of cotton-wool by 28.3%.

Table 2 – Cotton yield by applying mixed ligand complex as growth stimulants

№	Variants	Weight of cotton-wool (seeds and lint), in g / per 1 plant				Total harvest			
		harvest 1 28.08.16	harvest 2 14.09.16	harvest 3 30.09.16	Total	Sum of bolls, units per 1 plant	Weight of boll, g	Imma-ture fruit , g	%
1	$N_{200}P_{140}K_{60}$-background	80.25	22.97	10.8	114.6	26.00	4.4	19.30	100
2	Prepration 1	67.25	44.25	35.5	147.0	33.75	4.35	11.3	129.8

So, on the basis of the carried out studies it was revealed that Cu [(($PNBA)_2$+ ($MEA)_2$)] compound, has stimulating activity on the growth and development of cotton. In this metal complex, growth of bioactivity to almost 30% is observed.

Multifunctional action on plants, apparently, is associated with the activation of phytohormones, which is expressed in acceleration of seeds germination, plants lenght, mass of aboveground part and roots, productive bushiness. The revealed positive qualities of the stimulant under investigation ultimately lead to yield increase and an improvement in the cotton fiber quality.

Conclusion. Thus, our complex of agrochemical vegetative studies, the qualitative characteristics of the studied compound, and its influence on the yield of the tested plants made it possible to conclude that effective stimulant of a new generation that positively influenced the growth and development of cotton was obtained.

The practical significance of synthesized compounds is growing if we take into account that it is the mononuclear copper complex that exhibits maximum antifuzario activity [10]. To apply this compound as a growth preparation, the cotton seeds are soaked in advance by inoculation. Since *Fusarium* fungi are constantly present in the soil, the preparation simultaneously exhibits both growth and antifungicidal actions. In this regard, we can argue that an effective dual-action complex has been obtained that is promising in terms of introduction into agriculture.

REFERENCES

[1] Renfrew A.K. Transition metal complexes with bioactive ligands: mechanisms for selective ligand release and applications for drug delivery // Metallomics. 2014. Vol. 6. P. 1324-1335.

[2] Selvaganapathy M.M., Raman N. Pharmacological Activity of a Few Transition Metal Complexes: A Short Review // Journal of Chemical Biology & Therapeutics. 2016. Vol. 2, N 1.

[3] Shakir M., Hanif S., SherwaniA. M., Mohammad O., Al-Resayes SA (2015) Pharmacologically significant complexes of Mn(II), Co(II), Ni(II), Cu(II) and Zn(II) of novel Schiff base ligand, (E)-N-(furan-2-yl methylene) quinolin-8-amine: Synthesis, spectral, XRD, SEM, antimicrobial, antioxidant and in vitro cytotoxic studies// Journal of Molecular Structure. Vol. 1092. P. 143-159.

[4] Benzoic acids – Advances in Research and Application / Ed. Acton Q.A. Atlanta (USA): Scholarly editions, 2013.

[5] Ethanolamines – Advances in Research and Application. Edition. Eds. Q. Atlanta (USA): Scholarly editions, 2013.

[6] CrysAlisPro. Version 1.171.33.40. Oxford Diffraction (UK), 2007.

[7] Sheldrick G.M. Phase annealing in SHELX-90: direct methods for larger structures // ActaCrystallogr. A. 1990. Vol. 46. P. 467.

[8] Sheldrick G.M. SHELXL-97. Program for the Refinement of Crystal Structures. Göttingen (Germany): Univ. of Göttingen, 1997.

[9] Macrae C.F., Bruno I.J., Chisholm J.A. et al. // J. Appl. Cryst. 2008. Vol. 41. P. 4660.

[10] Ibragimov A.B., Ashurov Zh.M., Ibragimov A.B., Tashpulatov Zh.Zh. Sintez, stroenie i fungicidnaja aktivnost' mono- i bijadernogo smeshanno-ligandnogo kompleksa medi s p-nitrobenzojnoj kislotoj i monojetanolaminom // Koordinacionnaja himija. 2017. Vol. 43, N 6. P. 376-384.

[11] Ibragimov A.B., Zakirov B.S., Ashurov J.M. Crystal structure of the salt bis(triethanolamine-κ^3 N,O,O′)cobalt(II) bis[2-(2-oxo-2,3-dihydro-1,3-benzothiazol-3-yl)acetate] // ActaCrystallogr. E. 2016. Vol. 72. P. 502.

[12] Ibragimov A., Ashurov J., Ibragimov B. et. al. Synthesis, structure, and fungicidal activity of mono- and binuclear mixed-ligand copper complex with *p*-nitrobenzoic acid and monoethanolamine // J. Mol. Str. Vol. 1128, 15 January 2017. P. 307-316.

[13] Nonomura A.M., Nishio J.N., Benson A.A. Methods and compositions for enhancing plant growth with p-amino- or p-nitro-benzoic acids // US patent 5846908 A, 08.12.1998.

[14] Bergmann H. and Eckert H. Effect of monoethanolamine on growth and biomass formation of rye and barley // Plant Growth Regulation. 1990. Vol. 9. P. 1-8.

[15] Metodiki polevyh i vegetacionnyh opytov s hlopchatnikom. Tashkent: SojuzNIHI,1981. P. 368.

[16] Gajsin I.A., Reut V.I., Sagitova R.N., Hisameeva F.A., Ismailova A.I. Sostav dlja stimulirovanija rosta i razvitija sel'skohozjajstvennyh kul'tur. Patent RU 2261599 ot 10.10.2005.

[17] Keitt, G. W. Jr. Baker, R. A. Auxin activity of substituted benzoic acids and their effect on polar auxin transport // Plant Physiol. 1966. 41. P. 1561-1569.

[18] Crisan M, Bourosh P., Chumakov Y., Petric M., Ilia G. Supramolecular assembly and ab initio quantum chemical calculations of 2-hydroxyethylammonium salts of para-substituted benzoic acids // Crystal Growth & Design. 2012. Vol. 13(1). P. 143-154.

[19] Deutsch Z., Rubin-Preminger J.M., Bernstein J., Becker J.Y., Three crystal forms of tetrakis(μ2-2-nitrobenzoato-O,O′)-diaqua-di-copper(II) // CrystEngComm. 2006. Vol. 8. P. 41-50.

[20] Renfrew A.K. Transition metal complexes with bioactive ligands: mechanisms for selective ligand release and applications for drug delivery // Metallomics. 2014. Vol. 6. P. 1324-1335.

Резюме

А. Б. Ибрагимов, Л. Мамасалиева, Р. Ким, О. Мячина, Б. С. Zakirov,
Б. Т. Ибрагимов, Ж. М. Ашуров, А. А. Мамадрахимов

п-НИТРОБЕНЗОЙ ҚЫШҚЫЛЫ МЕН МОНОЭТАНОЛАМИНМЕН МЫСТЫҢ АРАЛАС ЛИГАНД КЕШЕНІНІҢ ҚҰРЫЛЫМЫ ЖӘНЕ БИОЛОГИЯЛЫҚ БЕЛСЕНДІЛІГІ

Түрлі өсімдік өсімін ынталандырғыштар қолданудың теориясы мен практикасының ағымдағы жай-күйін сараптау олардың минералдық тыңайтқыштар сияқты маңызды рөл атқаратын ауыл шаруашылығында олардың кеңінен қолданылатындығын атап өтуге мүмкіндік береді. Осыған байланысты, көптеген өсімді ынталандырғыштар жасалып, металл кешендеріне негізделген қосылыстар маңызды орын алуда.

Түйін сөздер: п-нитробензой қышқылы, моноэтаноламин, Cu кешені, молекулалық және кристалды құрылым, SAR, TG-DSK, масс спектр, өсімді ынталандыратын белсенділік.

Резюме

А. Б. Ибрагимов, Л. Мамасалиева, Р. Ким, О.Мячина, Б. С. Zakirov,
Б. Т. Ибрагимов, Ж. М. Ашуров, А. А. Мамадрахимов

СТРУКТУРА И БИОЛОГИЧЕСКАЯ АКТИВНОСТЬ
СМЕШАННО-ЛИГАНДНОГО КОМПЛЕКСА МЕДИ
С п-НИТРОБЕНЗОЙНОЙ КИСЛОТОЙ И МОНОЭТАНОЛАМИНОМ

Анализ современного состояния теории и практики применения различных стимуляторов роста позволяет отметить их широкое использование в сельском хозяйстве, где они играют важную роль как минеральные удобрения. В связи с этим создается множество стимуляторов роста, и соединения, основанные на металлических комплексах, занимают важное место.

Ключевые слова: п-нитробензойная кислота, моноэтаноламин, комплекс Cu, молекулярная и кристаллическая структура, SAR, TG-DSK, масс-спектр, стимулирующая рост активность.