Materials of Conferences

SYNTHESIS AND BIOLOGICAL ACTIVITY 1-METHYL-4-(2- TIOPIKOLINAMIN)-PIPERIDIN

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The article deals with the possibility of synthesis from waste of sulfur of oil industry of new biologically active connection 1-methyl-4-(2-tiopikolinamin) piperidin. On the basis of theoretical and experimental studies, the structure of the synthesized substance was proved and also its high growth stimulating activity related to vegetables (beets, carrots) and its ecological safety was revealed.

Nowadays one of the most priority places in the system of chemical assurance of agricultural plant cultivation production along with fertilizing and security facilities is occupied by growth stimulators. It's extremely important to find nontoxic highly effective preparation. In connection with toughening of ecological requirements the priority is given to low consumable, low toxic growth stimulating substances and preparations [1-3].

During many decades a number of scientific team groups have been working on creation of effective low toxic growth stimulating and crop capacity improving of agricultural plantings preparations. Among the variety of organic compounds the special place is occupied by heterocyclic, nitrogen-containing substances, which have a number of valuable biological features. One of the most important groups that deserves attention is hexamerous heterocyclic compounds, which contain piperidine cycles in its structure. They enter into the composition of many natural substances. Their application allows to regulate the most important processes in the plant organism purposefully, to realize potential facilities of the kind that are founded in genome by nature and selection more completely [4-5].

The aim of this work is the synthesis of sulfur-containing derivative piperidine series with the use of sulphuric wastes of oil industry and its compound, structure and biological activity examination.

Materials and methods of research. For the ascertainment of synthesized derivatives of piperidine, namely for identification of multiplication bond factor and composition of functional groups, there was used infrared spectroscopy. Infrared spectrums recorded on the device Specord-IR-75 in and around 4000-400 $см^{-1}$.

Toxicity of preparations was tested on white mice with the body weight of 17-22 g and rats with the body weight of 200-250 g, which were kept in conditions of vivarium according to norms of laboratory animals' feeding and keeping. Daily animal observation was carried out during 14 days. Animals that didn't perish during first 24 hours after preparation introduction were observed till the full recovery of behavior and appetite (not less than 72 hours). There were set the character and evidence of visual symptoms of poisoning, the speed of its coming and regression, lethality.

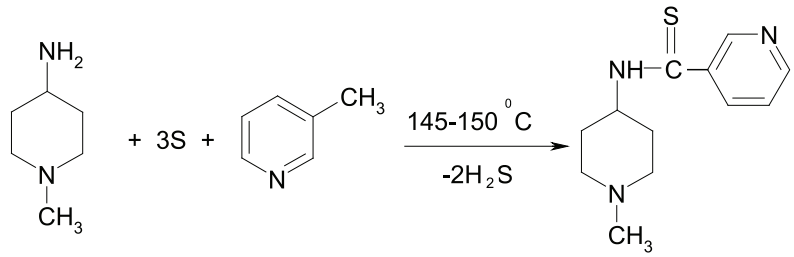
Solutions of preparation in different concentrations of 0,1 ml of water were introduced orally once into the stomach with the needle. To control animals there was introduced an analogical amount of sterile solution of known preparation of ciprofloxacin [6].

Experimental animals were divided into four equal groups, each group contained 10 animals. One group was control. Every group was observed, there was registered every incident of death and clinical demonstrations of toxic reactions on introduced doses of researched preparations.

On the base of preliminary experiments there were selected doses of the least and the greatest effect. By the minimal dose there wasn't observed the death of animals, and by the maximal dose there were 100% of deaths of experimental animals. After the ascertainment of minimal and maximal dose of preparations for the further experiments there were selected intermediate doses that are close to 50% of animal deaths.

Results and their discussion. **The process of synthesis of 1-methyl-4-(2-tiopikolinamin) piperidine.** Into the flask that was supplied with mechanical mixer, thermometer and reverse refrigerator there was put the mixture of 5 g (0,045 mole) of 1-methyl-4-aminopiperidine, 4,1 g (0,045 mole) of α-picoline and 4,3 g (0,135 mole) of sulphur. The reaction was carried out during 15 hours by the temperature of 145-150°C, with the control of thin-layer chromatography on the floating layer of aluminium oxide with the use of dissolvent from the mixture of benzol-acetone with their correlation of 5:1. After the end of reaction there was carried out an extraction of product with the use of chloroform as leach. For extract drying there is used calcined magnesium sulphate. After extract process the dissolvent is distilled off and the derived product 1-methyl-4-(2-tiopikolinamin) piperidin is weighed.

An implemented reaction of 1-methyl-4-(2-tiopikolinamin) piperidin synthesis progresses by the following scheme (practical output of product ≈75,5 %):



1-methyl-4-amino- sulphur ß-picoline piperidine 1-methyl-4-(2-tiopikolinamin) piperidine

While implementation of this reaction the taken mole correlation of initial substances is: 1-methyl-4-aminopiperidine: sulphur: 2-picolin = 1:3:1 considering admixtures corresponded to above mentioned reaction. The process of reaction was controlled with the use of thin-layer chromatography. Duration of reaction is 15 hours.

Empirical formula of synthesized compound according to the facts of element analysis can be presented as $C_{12}H_{17}N_2S$. Tiocompound has pale yellow colour, is well soluble in water, the temperature of melting is 115-117 °C.

On the base of facts of infrared spectroscopy there was proved the presence of connections C = S, C-N, N-C = S at the 1-methyl-4-(2-tiopikolinamin) piperidine.

An acute toxicity of preparation was estimated on the basis of indicator of LD_{50}, and also by the changing of clinical condition of animals during 4 days. The control of comparison is ciprofloxacin with the known value of toxicity of LD_{50} 176,2 ± 9,21 и 98,3 ± 8,6, accordingly, for mice and rats. Experimentally stated facts are showed in the Table 1.

Table 1

Acute toxicity of preparation

Preparation	LD_{50}, mg/kg	
	for mice, (M ± m)	for rats, (M ± m)
1-methyl-4-(2-tiopikolinamin) piperidine	225,3 ± 18,62	125,3 ± 14,6
Ciprofloxacin (standard)	176,2 ± 9,21	98,3 ± 8,6

As it's seen from the table 1, the toxicity of synthesized derivative piperidine is 1,3 times lower in comparison with standard – ciprofloxacin.

Thereby, as it follows from the experimentally stated facts 1-methyl-4-(2-tiopikolinamin) piperidine can be related to substances that have no pronounced toxicity.

An influence of 1-methyl-4-(2-tiopikolinamin) piperidine on the growth, harvest and the quality of beet and carrot. It was considered to be scientifically-practically interesting to study the influence of this synthesized compound on widely used crops – sugar beets and carrot. Usually a considerable influence of stimulator is observed from the very first stage of plant development, that's why the influence of researched compound was studied by force of carrying out of preplant treatment of seeds.

As it's known, the considerable role for the further development of any plant representative have deep changes that are in the seed embryo, which lead in the end to the changes of biological processes on the cell level duration. While this, the activity of ferments increases, the process of photosynthesis fastens, the content of carbohydrates in leaves increases and the produce ability becomes more active. In addition the acceleration of seed germination allows to avoid an oppressed action of weed to some degree.

On the base of experimental researches there is showed the possibility of change of plant harvest with the biologically-active substances. Change of growing processes depends on concentration of used preparations, and if while the low concentrations there is observed an accumulation of grow processes, than while the large ones, on the contrary, there is observed inhibition that means oppression. Results of experimental facts by the studying of the influence of different concentrations of researched compound on the energy of germination of carrot and beet, which were received while preplant treatment of seeds, are presented in Table 2.

Table 2

Energy of sprouting (numerator) and germination (denominator) of carrot and beet seeds while the treatment with the solutions of 1-methyl-4-(2-tiopikolinamin) piperidine

Concentration of preparation, %	Energy of sprouting and germination, %	
	carrot	beet
0	42/71	63/70
10^{-4}	55/91	63/92
10^{-3}	62/100	73/100
10^{-2}	50/89	67/83
10^{-1}	34/77	35/60

Maximum energy rise of seed sprouting of carrot and beet is observed in the interval of preparation concentration from 0,001 to 0,0001 %. While the preparation concentrations of 0,01 % the seed germination of researched plants becomes comparable to the control, and the inhibition of growth processes was stated higher this concentration. Preplant seed wetting in the compounds of 1-methyl-4-(2-tiopikolinamin) piperidine raise the energy of sprouting. The most optimal preparation concentration, which influences sprouting and germination of seeds, is concentration of 10^{-3} % Table 2). This concentration also influences the biochemical characteristics of carrot and beet while their complex treatment in the whole phase of development (Table 3-4).

While the wetting of seeds with the use of optimal concentration (0,001 %) of 1-methyl-4-(2-tiopikolinamin) piperidine solutions there was observed the active growth of roots and petioles of beet and carrot germs in comparison with control. Preplant treatment of seed material with the synthesized derivative of piperidine had a considerable influence on morphology not only of table beet, but also of carrot.

Plants that have grown from the seeds, which were treated with 1-methyl-4-(2-tiopikolinamin) piperidine, grow and develop better, enter the phase of root fall-off earlier, fascicular and economic ripeness occurs earlier too. More intensive increase of plant tops and assimilable surface of the leaves has a positive influence on root crop development (Table 4).

Table 3

Influence of 1-methyl-4-(2-tiopikolinamin) piperidine in the phase of root crop formation on the content of components in beet and carrot leaves, %

Types of preparation treatment of vegetables	Dry substances	Sugar	Chlorophyll
Control – complex treatment with water			
beet	12,0 ± 0,1	2,2 ± 0,05	25,9 ± 0,2
carrot	9,4 ± 0,1	3,5 ± 0,05	21,9 ± 0,2
Preplant seed treatment			
beet	12,7 ± 0,1	2,6 ± 0,05	33,0 ± 0,2
carrot	9,9 ± 0,1	3,7 ± 0,05	23.7 ± 0,2
Treatment only in phase of root crop formation			
beet	12,0 ± 0,1	2.7 ± 0,05	30,7 ± 0,2
carrot	10,1 ± 0,1	3,7 ± 0,05	22,9 ± 0,2
Complex treatment (preplant and in phase of root crop formation)			
beet	12,9 ± 0,1	2,9 ± 0,05	33,7 ± 0,2
carrot	10,5 ± 0,1	4,2 ± 0,05	24,0 ± 0,2

Table 4

Influence of 1-methyl-4-(2-tiopikolinamin) piperidine on the biometrical characteristics of root crops of beet and carrot

Variant	Length, cm	Diameter, cm	Index of root crop
Control (water)			
beet	10,8 ± 0,1	5,9 ± 0,2	1,83
carrot	14,0 ± 0,7	3,3 ± 0,1	4,23
1-methyl-4-(2-tiopikolinamin) piperidine			
beet	11,6 ± 0,2	6,8 ± 0,2	1,70
carrot	16,5 ± 0,7	4,0 ± 0,2	4,12

Thereby, while the beet and carrot seeds treatment with the solution of 1-methyl-4-(2-tiopikolinamin) piperidine there occurs an increase of plants' root system, square of leaf surface, acceleration of photosynthesis processes. At the same time photosynthesis as the base of plant grow and de-

velopment, accumulation of chemical compounds, and consequently of biomass, can be connected with other physiological characteristics, including the change of chemical composition. An increase of volume and mass of roots and root crops leads to the intensification of their absorbing ability and synthetic activity, and also of processes of ion and nourishing substances mass transfer along the plant, what promotes intensive growth of sprout and formation of the new organs.

Conclusion

1. There was developed a new way of receiving of the biologically active compound of 1-methyl-4-(2-tiopikolinamin) piperidine on the basis of sulphur waste of oil and gas products utilization. Its compound, structure and toxicity were stated.

2. There was revealed the stimulation of leaf-forming process, improvement of root crops' structure and increase of plant harvest by preplant treatment of seeds with 1-methyl-4-(2-tiopikolinamin) piperidine, and also positive influence of this tio-compound on the quality of carrot and beet.

3. New synthesized derivative of piperidine – 1-methyl-4-(2-tiopikolinamin) piperidine is ecologically safe and can be recommended as the regulator of growth for beet and carrot.

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