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FUNGICIDAL PROPERTIES OF N-(p-CARBOXYPHENYL)IMIDE-2,3-DICHLOROBICYCLO-[2.2.1]HEPT-5-EN-2,3-DICARBOXYLIC ACID**Y.M.Nagiev***M.Nagiyev Institute of Catalysis and Inorganic Chemistry, NAS of Azerbaijan**yaqub56@mail.ru*

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As a result of the interaction of substituted aminobenzoic acids and dichloromaleic anhydride in glacial acetic acid, various N-substituted imides of dichloromaleic acid have been obtained. Based on the diene synthesis of cyclopentadiene and N-substituted imides of dichloromaleic acid, N-(*orthometa*- and *para*-carboxyphenyl)imides of 2,3-dichlorocyclo-[2.2.1]hept-5-ene-2,3-dicarboxylic acid have been synthesized. The obtained imides have been tested as a potential effective complex biologically active drug. The results of multiple tests have demonstrated that these compounds possess, simultaneously, high fungicidal and bactericidal activity against cotton *verticillium wilt*. So, for a concentration of 0.1%, the obtained compounds almost completely destroy the fungus *verticillium dahliae*, as well as thionic iron-oxidizing and sulfate-reducing aerobic bacteria VKM V-458 and VKM V-1388.

Keywords: aminobenzoic acid, imide, biological tests, fungicidal activity, cotton wilt, concentration.

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Introduction

The problem of chemical plant protection in agriculture is actual significance. The search for effective fungicides, herbicides, pesticides, bactericides and other chemical agents for combating plant diseases is entering in the new phase: compounds with a complex mechanism of action are required. The general drugs do not have a complex effect and to prevent the mutation of microbes and bacteria, substances with a complex composition and effect are required, that is, for example, both fungicidal and bactericidal ones.

The mechanism of action of most fungicides is known only in general terms. Most often, fungicides act on fungi directly, interfering into biochemical reactions occurred in fungal cells, or by blocking the enzymes that control these reactions [1].

Bactericides exert a strong inhibitory effect on the growth and reproduction of bacteria without damaging the cells of macroorganisms [2, 3].

Fusarium wilt is a specific disease of fine-fiber cotton varieties caused by the soil fungus *Fusarium oxysporum f. Vasinfectum Bilai*. This disease is difficult to treat with conventional remedies.

During current studying, various N-substituted imides of dichloromaleic acid have

been used for the treatment of *Fusarium wilt*. These compounds have proven effective as complex chemical agents, the molecular structure of which has various strong biologically active fragments.

The compounds of the bicycle-[2.2.1]-hept- and [2.2.2]oct-5-ene series are known to have a wide spectrum of biological and physiological action [4–9, 12] and, accordingly, our works [4, 6, 8, 10, 11, 13], devoted to the study of the reaction of diene synthesis of N-aryldichloromaleinimides with cyclopentadiene (CPD), have shown that the obtained compounds are included in the sphere of action of these compounds.

The present work is devoted to the synthesis of new mono- and bicyclic compounds based on *ortho*-, *meta*- and *para*-aminobenzoic acid, using dichloromaleic anhydride and cyclopentadiene (CPD), and to their study as effective chemical plant protection agents.

Experimental part

Based on the primary isomers of aminobenzoic acid and dichloromaleic anhydride (DCMA), N-*ortho*-, *meta*- and *para*-carboxyphenylimide of dichloromaleic acid was synthesized. The reaction proceeds in two stages: in the first stage an amido acid is formed, it

under reaction conditions, further cycles to form an imide. Therefore, in the second stage, under carrying out the reaction of diene synthesis with the participation of such a dienophile, cyclopentadienediene was expediently chosen as a strong electron donor reagent.

The reaction proceeds according to I and II schemes:

Scheme 1.

R = a = o-C₆H₄COOH, b = m-C₆H₄COOH, c = p-C₆H₄COOH.

Scheme 2.

R = a = o-COOH, b = m-COOH, c = p-COOH.

A detailed study of this reaction and the resulting products are given in [14]. Using X-ray diffraction analysis and NMR method it was shown that the resulting adducts have an *endo* configuration [15–19].

Results and discussion

In order to find out whether the new adducts synthesized by us on the basis of N-substituted imides of dichloromaleic acid have biologically active properties, they have been tested in many ways.

The fungicidal and bactericidal activity of the compounds was investigated by suppressing (inhibiting) the germination of spores and mycelium on the *Fusarium solani* (F.S.), *Helminthosporium sativum* (H.S.), *Botrytis sinera* (B.S.) fungi and on the *Xanthomonas malvacearum* (X.M.) bacteria. The results showed that one of the compounds has fungicidal activity (Table 1).

Tests of the compounds for the presence of plant growth stimulating activity of the preparations synthesized by us were carried out in vitro, using wheat and cucumber seedlings (Table 2).

As is seen from obtained data, the compounds demonstrated stimulating activity only on wheat germs and cucumbers germs are inhibited. According to the data obtained (Table 3), the compounds exhibited stimulating activity only on wheat, while cucumber seedlings were inhibited.

The biocidal activity of the compounds was determined using pure cultures of *Tnibocillus ferrooxians* BKM B-458 aerobic iron-oxidizing thionic bacteria and *Desulfovibrio acsulfuricans* BKM B-1388 anaerobic sulfate-reducing bacteria. The test results are given in Tables 4 and 5, respectively.

Table 1. Fungicidal and bactericidal activity of *N-meta*- and *N-para*-carboxyphenylimide compounds

Name of a compound	Inhibition of spore germination, mass %			Inhibition of mycelial growth, mass %			Inhibition of bacterial activity, mass %
	mass share of the dissolved substance						
	0.005			0.003			0.003
N-(<i>m</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	65.9	85.8	–	0	30.6	–	2.1
N-(<i>p</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	71.5	87.9	–	14.9	48.6	–	22.8
TMTD standard	100.0	100.0	100.0	100.0	100.0	100.0	100.0

Table 2. The results of biological tests of N-(*m*-carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid on stimulating plant growth

Name of a compound	Dose, g/ton	The length of seedlings,%	
		wheat	cucumbers
N-(<i>m</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	1	108	85
	10	117	70
Control	–	100	100

Table 3. The results of tests on the biocidal activity of the compounds for VKM B-458 thionic iron-oxidizing aerobic bacteria

Name of a Compound	The concentration of the compound, mass %				
	0.0001	0.001	0.01	0.1	1.0
N-(<i>m</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	+	+	–	–	–
N-(<i>p</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	+	+	–	–	–

Note: "+" – growth of bacteria, "-" – lack of growth.

Table 4. Test results of compounds against the VKM B-1388 sulfate-reducing aerobic bacteria

Name of a Compound	The concentration of the compound, mass %				
	0.0001	0.001	0.01	0.1	1.0
N-(<i>m</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	+	+	+	–	–
N-(<i>p</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	+	+	+	–	–

Note: "+" – growth of bacteria, "-" – lack of growth.

Table 5. The results of a study of the fungicidal activity of N-(*p*-Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid against verticilliosis cotton wilt

Experiments	Concentration %	Growth and development of fungus verticillium dahlial in mm for 1 month (control after 24 hours)									
		09	11	13	16	18	20	23	25	27	30
N-(<i>p</i> -Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-ene-2,3-dicarboxylic acid	0.01	–	–	–	0.3	0.5	0.8	10	16	21	24
	0.05	–	–	–	0.3	0.5	0.8	11	17	21	24
	0.1	–	–	–	–	–	–	–	–	–	–
Control with no drugs added	–	0.8	10	12	13	16	27	36	50	55	60

From the data given in Tables 3 and 4, it can be seen that the compounds studied process biocidal activity against thionic and sulfate-reducing bacteria, i.e. the compounds given are bactericides.

Thus, the tests carried out revealed that the synthesized compounds are of certain useful properties (biocidal, fungicidal, herbicidal, anthelmintic), that allows to recommend the obtained compounds as new biologically active substances.

In the laboratory at the Azerbaijan Scientific Research Institute of Plant Protection, a series of synthesized adducts was tested as fungicides against verticillium cotton wilt, caused by *verticillium dahlia*.

The fungicidal properties of the compounds were studied by method growing the causative agent of cotton wilt on an agarized beer wort medium in the presence of N-(p-Carboxyphenyl)imide-2,3-dichlorobicyclo[2.2.1]hept-5-en-2,3-dicarboxylic acid.

The medium with various concentrations (0.1, 0.05, 0.01% ai) of the preparations was sterilized and poured with a thin layer evenly into Petri dishes. After that, a pure culture of the wilt causative agent – *verticillium dahlia* – was applied to the solidified nutrient medium, in the center of Petri dishes, which were placed into a thermostat and kept there at a temperature of 25–26°C.

Starting from the third day after trial establishment and then every other day, using the strip of graph paper, we measured the growth intensity of the mycelium of the *verticillium dahlia* fungus.

The control was Petri dishes with agar medium of beer wort without any preparation in it. The experiment was repeated three times. An analysis of the obtained results showed that out from of the number of investigated compounds, only N-(p-Carboxyphenyl)imide-2,3-dichlorobicyclo [2.2.1]hept-5-ene-2,3-dicarboxylic acid has a high fungicidal activity against cotton verticillosis wilt. The test results are presented in Table 5.

From the obtained data given in Table 5, the studied drug in all tested concentrations significantly inhibits growth and stops the development of the verticillum dahlia fungus. For a

concentration of 0.1%, it shows a killing effect on the verticillum dahlia fungus. In this embodiment, germination of the fungus mycelium was not observed at all.

So, at a concentration of 0.1%, they almost completely destroy the verticillum dahliae fungus, as well as thionic iron-oxidizing and sulfate-reducing aerobic bacteria VKM V-458 and VKM V-1388.

Also, in the helminthology laboratory of the Azerbaijan Scientific Research Veterinary Institute, a number of synthesized compounds has been tested as antihelmintics for fatsiol in vitro. The test results showed that N-(p-Carboxyphenyl)imide-2,3-dichlorobicyclo-[2.2.1]hept-5-ene-2,3-dicarboxylic acid has in vitro anthelmintic efficacy and it is of great interest for further studies as anthelmintics in the body of experimental animals.

Thus, it was found that the compound of N-(p-Carboxyphenyl)imide-2,3-dichlorobicyclo-[2.2.1]hept-5-en-2,3-dicarboxylic acid had a high fungicidal activity against verticillosis cotton wilt, which allows us to recommend it as a new biologically active substance.

Conclusions

1. Based on cyclopentadiene and N-substituted imides of *dichloromaleic acid*, the N-(*ortho-meta-para-carboxyphenyl*)imides of 2,3-dichlorocyclo-[2.2.1]hept-5-en-2,3-dicarboxylic acids have been synthesized and described.
2. The synthesized compounds have been tested in regard to potential biologically active properties: biocidal, fungicidal, herbicidal, anthelmintic.
3. It has been found for the first time that N-(p-carboxyphenyl)imide of- 2,3-dichlorobicyclo-[2.2.1]hept-5-en-2,3-dicarboxylic acids reveals ultra-high simultaneous fungicidal and bactericidal activity against verticillosis cotton wilt and can be recommended as an effective remedy against this disease in the field scale.

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N-(p-CARBOXYPHENYL)İMİD-2,3-DİHLOROBİCİCLO-[2.2.1]HEPT-5-EN-2,3-DİKARBON TURŞUSUNUN FUNGİSİD XÜSUSİYYƏTLƏRİ

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Ortho-, meta-, paraaminobenzoy turşusu və dixloromalein anhidridinə əsaslanaraq, buzlu sirkə turşusu mühitində, dixloromalein turşusunun N əvəzli imidləri alınır. N-(orto-meta- və para-karboksifenil)imid-2,3-dixlorobisiklo[2.2.1]hept-5-en-2,3-dikarbon turşusunun sintezi üçün, dixloromalein turşusunun N əvəzli imidləri tsiklopentadienlə dien sintezi reaksiyasına daxil edilmişdir. Sintez edilmiş maddələrin quruluşları müasir fizik-kimyəvi metodlarla təsdiqlənir. Dichloromalein turşusu və tsiklopentadienin N-əvəzli imidləri əsasında sintez etdiyimiz yeni birləşmələrin müəyyən praktik xüsusiyyətlərə malik olub-olmadığını öyrənmək üçün kənd təsərrüfatında hərtərəfli sınaqdan keçirilmiş və müxtəlif qatılıqlarda bioloji aktivlikləri öyrənilmişdir. Çoxsaylı test nəticələri göstərdi ki, sintez edilmiş adduktlar arasında N-(p-karboksifenil)imid-2,3-dixlorobisiklo-[2.2.1] hept-5-en-2,3-dikarbon turşusu, pambıq bitkisinin əmələ gələn vilt

xəstəliyinə qarşı çox yüksək fungusid aktivliyinə malikdir. Xüsusilə qeyd etmək lazımdır ki, alınan maddə 0.1% qatılığında *verticillium dahlial* göbələklərinin tamamilə məhv olmasına səbəb olur.

Açar sözlər: aminobenzoy turşusu, imide, bioloji testlər, fungusid aktivliyi, pambıq yarası, konsentrasiyası.

**ФУНГИЦИДНЫЕ СВОЙСТВА N-(*n*-КАРБОКСИФЕНИЛ)ИМИДА-2,3-ДИХЛОРБИЦИКЛО-
[2.2.1]ГЕПТ-5-ЕН-2,3-ДИКАРБОНОВОЙ КИСЛОТЫ**

Я.М.Нагиев

На основе *орто*-, *мета*- и *пара*-аминобензойной кислоты и с использованием дихлормалеинового ангидрида в среде ледяной уксусной кислоты получены N-замещенные имида дихлормалеиновой кислоты. Для синтеза N-(*орто*- *мета*- и *пара*- карбоксифенил)имида-2,3-дихлорбицикло-[2.2.1]гепт-5-ен-2,3-дикарбоновой кислоты были использованы N-замещенные имида дихлормалеиновой кислоты, а в качестве диена цикlopentadiен. Структуры синтезированных аддуктов подтверждены современными физико-химическими методами. С целью выяснения того, обладают ли синтезированные нами новые аддукты на основе N-замещенных имидов дихлормалеиновой кислоты и цикlopentadiена определенными практическими свойствами, были проведены их разносторонние испытания в сельской хозяйстве, а также изучены их биологические активности в разных концентрациях. Результаты многократных испытаний показали, что из среди синтезированных аддуктов N-(*n*-карбоксифенил)имид-2,3-дихлорбицикло-[2.2.1]гепт-5-ен-2,3-дикарбоновой кислоты обладает очень высокой фунгицидной активностью против вертициллезного вилта хлопчатника. Особенно, надо отметить, что в концентрации 0.1% он показывает убивающее действие на гриб *verticillium dahlial*.

Ключевые слова: аминобензойная кислота, имид, биологические испытания, фунгицидная активность, вилт хлопчатника, концентрация.