**ХИМИЧЕСКИЕ НАУКИ / CHEMICAL SCIENCES**
**Оригинальная статья / Original article**
**УДК 632.9: 547.835.5**
**DOI: 10.21285/2227-2925-2017-7-1-16-20**

# СИНТЕЗ И БИОЛОГИЧЕСКИЕ ИСПЫТАНИЯ НА ПЕСТИЦИДНУЮ АКТИВНОСТЬ ПРОИЗВОДНЫХ 1,2,3,4,5,6,7,8,9,10-ДЕКАГИДРОАКРИДИНДИОНА-1,8

**© А.Н. Пырко**

Международный государственный экологический институт имени А.Д. Сахарова
Белорусского государственного университета,
Республика Беларусь, 220070, г. Минск, ул. Долгобродская, 23/1.

*Целью работы является синтез и испытание на пестицидную активность производных декагидроакридиндиона, которые могли бы стать основой средств защиты растений. Исследованные соединения получены трехкомпонентной гетероциклизацией первичных аминов, ароматических альдегидов и димедона. Синтезированные соединения были испытаны на некоторые виды инсектицидной (против toxoptera graminum, musca domestica,meloidogyne incognita, heliothis virescens, diabrotica undecimpunctata howardi, caenorhabditis elegans), фунгицидной (против drechslera, erysiphe, puccinia, peronospora) и гербицидной активности (против amaranthus retroflexus, brassica rapa, abutilon theophrasti, alopecurus myosuroides, avena fatua, echinochloa crus galli). Все соединения проявили инсектицидную активность против toxoptera graminum. Три соединения проявили гербицидную активность против amaranthus retroflexus. Только одно соединение из шести проявило фунгицидную активность против drechslera.*
*Ключевые слова: производные декагидроакридина, синтез, пестицидная активность*

**Формат цитирования:** Пырко А.Н. Синтез и биологические испытания на пестицидную активность производных 1,2,3,4,5,6,7,8,9,10-декагидроакридиндиона-1,8 // Известия вузов. Прикладная химия и биотехнология. 2017. Т. 7, N 2. С. 16–20. DOI: 10.21285/2227-2925-2017-7-1-16-20

# SYNTHESIS AND BIOLOGICAL TESTING FOR PESTICIDAL ACTIVITY OF 9-ARYL-N-ARYL, ALKYL-SUBSTITUTED 1,2,3,4,5,6,7,8,9,10-DECAHYDROACRIDINE-1,8-DIONE DERIVATIVES

**© A.N. Pyrko**

International Sakharov Environmental Institute Belarussian State University,
23/1, Dolgobrodskaya St., Minsk, 220070, Republic of Belarus.

*The purpose of this work is the synthesis and pesticidal activity testing of 9-aryl-N-aryl, alkyl-substituted 1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione derivatives which could become the basis of plant protection products. The substances investigated were obtained by three-component heterocyclization of primary amines with aromatic aldehydes and dimedone. The synthesized compounds were tested for certain types of insecticide (against toxoptera graminum, musca domestica, meloidogyne incognita, heliothis virescens, diabrotica undecimpunctata howardi, caenorhabditis elegans), fungicidal (against drechslera, erysiphe, puccinia, peronospora) and herbicidal (against amaranthus retroflexus, brassica rapa, abutilon theophrasti, alopecurus myosuroides , avena fatua, echinochloa crus galli) activities. All synthesized compounds have shown promising insecticidal activities against toxoptera graminum. 9-(4-methoxyphenyl)-, N-2-phenylethyl-substituted, 9-(3,4-methoxyphenyl)-, N-2-carboxyethyl-substituted and 9-(2-hydroxyphenyl)-N-octyl-substituted derivatives have shown significant herbicidal activities against amaranthus retroflexus. 9-phenyl-N-methyl-substituted derivative was active against amaranthus retroflexus, brassica rapa, and abutilon theophrasti. Only this compound showed antifungal activity against drechslera.*
*Keywords: decahydroacridinedione derivatives, synthesis, pesticidal activity*

**For citation:** Pyrko A.N. Synthesis and Biological Testing for Pesticidal Activity of 9-aryl-n-aryl, alkyl-substituted 1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione Derivatives. *Izvestiya Vuzov. Prikladnaya Khimiya I Biotekhnologia* [Proceeding of Universities. Applied Chemistry and Biotechnology]. 2017, vol. 7, no. 2 , pp. 16–20 (in Russian). DOI: 10.21285/2227-2925-2017-7-2-16-20

**INTRODUCTION**

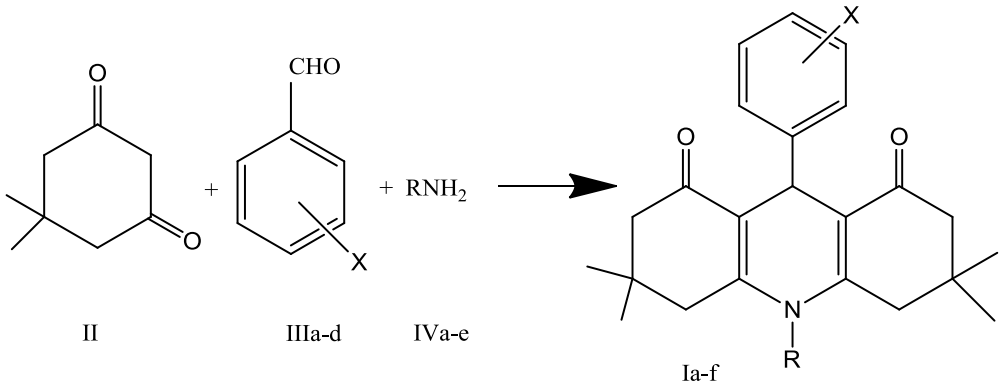
Decahydroacridinediones containing the 1,4-dihydropyridine fragment can be obtained by the Hantzsch synthesis [1–4]. These compounds reveal a broad spectrum of biological activities [5, 6]. The dyes of the decahydroacridine series have been studied to apply them as laser dyes and fluorescent marks [7].

The present paper describes the studies on synthesis and pesticide testing for decahydroacridinediones (Ia-f).

**METHODS AND RESULTS**

The substances under study were obtained based on the three-component heterocyclization of primary amines (IVa-e), aldehydes (IIIa-d) and dimedone (II). The cyclization is due to heating of equimolar quantities of dimedone and amine in the solution of glacial acetic acid with addition of aromatic acetaldehydes. The chemical structures of synthesized compounds were identified using physical, elemental and spectroscopic analyses. The results were summarized in Table 1.

Scheme 1




X = H (IIIa, Ia,b), 3,4-OMe (IIIb, Ic,f), 4-OMe (IIIc, Id), 2-OH (IIId, Ie); R = Me (IVa, Ia), Ph (IVb, Ib,c), $CH_2CH_2Ph$ (IVc, Id), $(CH_2)_7Me$ (IVd, Ie), $CH_2CH_2CO_2H$ (IIId, If)

***Table 1***

***Physical and chemical characteristics of synthesized compounds (Ia-e)***

| Compound | R | X | Molecular formula | Melting point from EtOH, °C | Yield, % | UV spectrum, EtOH, $\lambda_{max.}$, nm, (lgε) |
|---|---|---|---|---|---|---|
| Ia | 9-phenyl-3,3,6,6,10-pentamethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione | | | | | |
| | Me | H | $C_{24}H_{29}O_2N$ | 236-238 | 87 | 253 (4.23), 276 (4.15), 377 (3.81) |
| Ib | 9,10-diphenyl-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione | | | | | |
| | Ph | H | $C_{29}H_{31}O_2N$ | 235-237 | 85 | 254 (4.23), 271 (4.11), 378 (3.78) |
| Ic | 9-(3,4-dimethoxyphenyl)-10-phenyl-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1.8-dione | | | | | |
| | Ph | 3,4-OMe | $C_{31}H_{35}O_4N$ | 187-199 | 88 | 254 (4.41), 271 (4.12), 377 (3.85) |
| Id | 9-(4-methoxyphenyl)-10-(2-phenylethyl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione | | | | | |
| | $CH_2CH_2Ph$ | 4-OMe | $C_{32}H_{37}O_3N$ | 211-213 | 84 | 255 (4.25), 272 (4.38), 381 (3.92) |
| Ie | 9-(2-hydroxyphenyl)-10-octyl-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione | | | | | |
| | $(CH_2)_7Me$ | 2-OH | $C_{31}H_{43}O_3N$ | 116-118 | 82 | 254 (4.31), 272 (4.28), 379 (3.90) |
| If | 9-(3,4-methoxyphenyl)-10-(2-carboxyethyl)-3,3,6,6-tetramethyl-1,2,3,4,5,6,7,8,9,10-decahydroacridine-1,8-dione | | | | | |
| | $CH_2CH_2CO_2H$ | 3,4-OMe | $C_{28}H_{35}O_6N$ | 215-217 | 83 | 253 (4.29), 273 (4.16), 378 (3.91) |

**General procedure for decahydroacridinediones (Ia-f) synthesis**

A mixture of dimedone (2.80 g, 20 mmol) and amine (10 mmol) in 20 ml glacial acetic acid was being heated for 30 min, then benzaldehyde (10 mmol) was added, and the mixture was heated for additional
1.5 h. The solvent was boiled out, and the residue was recrystallized from ethanol.

**Biological testing**

Pesticide testing involved identification of insecticides (insect killers including adults, ova, and larvae) , fungicides and phytotoxins (herbicides).

Fungus greenhouse tests were carried out by spraying substances on plants which were further inoculated with *drechslera, erysiphe, puccinia, peronospora*.

The compound efficiency was assessed by comparing sprayed and non-sprayed plants. The results are shown in Table 2.

Insect pests are a major factor of agricultural crops loss. Insecticidal activity of compounds (Ia-f) *toxoptera graminum, musca domestica,meloidogyne incognita, heliothis virescens, diabrotica undecimpunctata howardi, caenorhabditis elegans* was tested. The results are shown in Table 3.

***Table 2***

***Data on antifungal activity of synthesized compounds***

| compound | Dose, ppm | Name of fungus and greenhouse test result | | | |
|---|---|---|---|---|---|
| | | drechslera | erysiphe | puccinia | peronospora |
| Ia | 100.00 | 50 | 0 | 0 | 0 |
| Ib | 100.00 | 0 | 0 | 0 | 0 |
| Ic | 100.00 | 0 | 0 | 0 | 0 |
| Id | 100.00 | 0 | 0 | 0 | 0 |
| Ie | 100.00 | 0 | 0 | 0 | 0 |

note: 100 – The product is active. It causes more than 80% inhibition of fungus development;
50 – The product is slightly active. It causes 50-80% inhibition of fungus development;
0 – The compound is regarded as inactive. It causes less than 50% inhibition of fungus development.

***Table 3***

***Data on insecticidal activity of synthesized compounds***

| Compound, biological effect Ia | plant | days | dose | unites | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | | | | | Ia | Ib | Ic | Id | Ie | If |
| Toxoptera graminum, mixed | sorghum | 6 | 0.1 | ppm | 3 | 5 | 3 | 5 | 5 | 3 |
| Musca domestica, pupae | – | 6 | 1.0 | ug/well | 1 | 1 | 1 | 1 | 1 | 1 |
| Meloidogyne incognita, J2 | – | 5 | 5.0 | ppm | 1 | 1 | 1 | 1 | 1 | 1 |
| Heliothis virescens, egg | – | 8 | 0.6 | ug/ well | 1 | 1 | 1 | 1 | 1 | 1 |
| | | 6 | | | 1 | 1 | 1 | 1 | 1 | 1 |
| Diabrotica undecimpunctata howardi, egg | cucumber | 6 | 0.3 | ppm | 1 | 1 | 1 | 1 | 1 | 5 |
| Caenorhabditis elegans, mixed | E.coli | 7 | 5.0 | | 1 | 1 | 1 | 1 | 1 | 1 |

note: 1 – 0–29% observed insect death rate; 3 – 30–69% observed insect death rate; 5 – 70–100% observed insect death rate.

***Table 4***

***Data on herbicidal activity of synthesized compounds***

| Plant | Dose, ppm | Compound, Biological effect, % | | | | | |
|---|---|---|---|---|---|---|---|
| | | Ia | Ib | Ic | Id | Ie | If |
| Amaranthus retroflexus | 100 | 30 | 0 | 0 | 70 | 70 | 90 |
| Brassica rapa | 100 | 10 | 0 | 0 | 0 | 10 | 0 |
| Abutilon theophrasti | 100 | 30 | 0 | 0 | 0 | 0 | 0 |
| Alopecurus myosuroides | 100 | 0 | 0 | 0 | 0 | 0 | 0 |
| Avena fatua | 100 | 0 | 0 | 0 | 0 | 0 | 0 |
| Echinochloa crus galli | 100 | 0 | 0 | 0 | 0 | 0 | 0 |

Herbicidal activity of compounds against *amaranthus retroflexus, brassica rapa, abutilon theophrasti, alopecurus myosuroides, avena fatua, echinochloa crus galli* was studied The results are shown in Table 4 and expressed in death rate percentage towards non-sprayed plants.

**CONCLUSION**

Thus, the present study described the method for synthesis of 9-aryl-N-aryl, alkyl-substituted 1,2,3,4,5,6,7,8,9,10-decahydroacridine-1.8-dione derivatives through the three-component heterocyclization of primary amines with aromatic aldehydes and dimedone.

All synthesized compounds showed insecticidal activity against *toxoptera graminum..* 9-(4-Methoxyphenyl)-, N-2-phenylethyl-substituted, 9-(3,4-methoxyphenyl)-, N-2-carboxyethyl-substituted and 9-(2-hydroxyphenyl)-N-octyl-substituted compunds showed significant herbicidal activity against *amaranthus retroflexus.* 9-Phenyl-,N-methyl-substituted derivative was active against *amaranthus retroflexus, brassica rapa,* and *abutilon theophrasti.* Only that compound showed antifungal activity against *drechslera.*

**БИБЛИОГРАФИЧЕСКИЙ СПИСОК**

**1.** Safaei-Ghomi J., Ghasemzadeh M. A., Zahedi S. ZnO nanoparticles: a highly effective and readily recyclable catalyst for the one-pot synthesis of 1, 8-dioxodecahydroacridine and dioxooctahydroxanthene derivatives //Journal of the Mexican Chemical Society. 2013. V. 57, N. 1. P. 1–7.

**2.** Nakhi A., Srinivas P. T. V., Rahman M. S. Amberlite IR-120H catalyzed MCR: design, synthesis and crystal structure analysis of 1, 8-dioxodecahydroacridines as potential inhibitors of sirtuins //Bioorganic and Medicinal Chemistry Letters. 2013. V. 23, N. 6. P. 1828–1833.

**3.** Pyrko A.N. Synthesis and Transformations of New 1,2,3,4,5,6,7,8,9,10-Deca-hydroacridine-1,8-dione Derivatives // Russian Journal of Organic Chemistry. 2008. V. 44, N. 8. P. 1215–1224.

**4.** Kumar A., Sharma S. A grinding-induced catalyst- and solvent-free synthesis of highly functionalized 1,4-dihydropyridines via a domino multicomponent reaction // Green Chem. 2011. Vol. 13. P. 2017–2020.

**5.** To Q. H., Lee Y. R., Kim S. H. Efficient one-pot synthesis of acridinediones by indium(III) triflate-catalyzed reactions of β-enaminones, aldehydes, and cyclic 1,3-dicarbonyls // Bulletin of the Korean Chemical Society. 2012. Vol. 33, N. 4. P. 1170–1176.

**6.** Shchekotikhin Yu.M., Nikolaeva T.G., Shub G.M., Kriven'ko A.P.Synthesis and antibacterial activity of substituted 1,8-dioxodecahydroacridines // Khim.-Farm. Zh. 2001. V. 35, N 4. P. 206–211.

**7.** Gutsulyak Kh. V., Manzhara V. S., Mel'nik M. V., Kalinc T. I. Relationship between the structure and photostability of decahydroacridine derivatives // J. Appl. Spectr. 2005. Vol. 72, No. 4. P. 488–494.

**REFERENCES**

**1.** Safaei-Ghomi J., Ghasemzadeh M.A., Zahedi S. ZnO nanoparticles: a highly effective and readily recyclable catalyst for the one-pot synthesis of 1,8-dioxodecahydroacridine and dioxooctahydroxanthene derivatives. *Journal of the Mexican Chemical Society*. 2013, vol. 57, no. 1, pp. 1–7.

**2.** Nakhi A., Srinivas P.V., Rahman M.S. Amberlite IR-120H catalyzed MCR: design, synthesis and crystal structure analysis of 1,8-dioxodecahydroacridines as potential inhibitors of sirtuins. *Bioorganic and Medicinal Chemistry Letters*. 2013, vol. 23, no.6. pp. 1828–1833.

**3.** *Pyrko A.N.* Synthesis and Transformations of New 1,2,3,4,5,6,7,8,9,10-Deca hydroacridine-1,8-dione Derivatives. *Russian Journal of Organic Chemistry*. 2008, vol. 44, no. 8, pp. 1215–1224.

**4.** Kumar A*.,* Sharma S. A grinding-induced catalyst- and solvent-free synthesis of highly functionalized 1,4-dihydropyridines via a domino multicomponent reaction. *Green Chem*. 2011, vol. 13, pp. 2017–2020.

**5.** To Q.H., LeeY.R., Kim S.H. Efficient one-pot synthesis of acridinediones by indium(III) triflate-catalyzed reactions of β-enaminones, aldehydes, and cyclic 1,3-dicarbonyls. *Bulletin of the Korean Chemical Society.* 2012, vol. 33, no. 4, pp. 1170–1176.

**6.** Shchekotikhin Yu.M., Nikolaeva T.G., Shub G.M., Kriven'ko A.P. Synthesis and antibacterial activity of substituted 1,8-dioxodecahydroacridines. *Khim.-Farm. Zh.* 2001, vol. 35, no. 4, pp. 206–211.

**7.** Gutsulyak Kh.V., Manzhara M.V., Mel'nik V.S., Kalinc T.I. Relationship between the structure and photostability of decahydroacridine derivatives. *J. Appl. Spectr*. 2005, vol. 72, no. 4, pp. 488–494.

**Критерии авторства**

Пырко А.Н. выполнил экспериментальную работу, на основании полученных результа-

***Contribution***

Pyrko A.N. carried out the experimental work, on the basis of the results summarized the material

тов провел обобщение и написал рукопись. Пырко А.Н. имеет на статью авторские права и несет ответственность за плагиат.

***Конфликт интересов***

Автор заявляет об отсутствии конфликта интересов.

***СВЕДЕНИЯ ОБ АВТОРАХ***
***Принадлежность к организации***

**Анатолий Н. Пырко**
Международный государственный экологический институт имени А.Д. Сахарова
Белорусского государственного университета
К.х.н., доцент кафедры биохимии
и биофизики
pyrko@yandex.ru

***Поступила 21.09.2016***

and wrote the manuscript. Pyrko A.N. have author's rights and bear responsibility for plagiarism.

***Conflict of interests***

The author declare no conflict of interests regarding the publication of this article.

***AUTHORS' INDEX***
***Affiliation***

**Anatolii N. Pyrko**
International Sakharov Environmental Institute
Belarussian State University
Ph.D. (Chemistry),
Associate Professor
pyrko@yandex.ru

***Received 21.09.2016***